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Review Article

Contemporary management of ventricular arrhythmias in heart failure

Ourania Kariki[1], Maximos Georgopoulos[1], Nikitas Katsillis[1], Anastasios Chatziantoniou[1], Stavroula Koskina[1], Andromahi Zygouri[1], Athanasios Saplaouras[1], George Bazoukis[2], Aggeliki Gkouziouta[1], Konstantinos Vlachos[1], Stylianos Dragasis[1], Panagiotis Mililis[1], Stamatis Adamopoulos[1], Michael Efremidis[1], Konstantinos P Letsas[1]

[1]Department of Cardiology, Onassis Cardiac Surgery Center, Athens, Greece; [2]Department of Cardiology, Larnaca General Hospital, Larnaca, Cyprus

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Abstract: Enhanced ventricular arrhythmogenesis is commonly experienced by patients in the end-stage of heart failure spectrum. A high burden of ventricular arrhythmias can affect the ventricular systolic function, lead to unexpected hospitalizations and further deteriorate the prognosis. Management of ventricular arrhythmias in this population is challenging. Implantable cardioverter-defibrillators are protective for the immediate termination of life-threatening arrhythmias but they have no impact in reducing the arrhythmic burden. Combination treatment with invasive (catheter ablation, mechanical hemodynamic support, sympathetic denervation) and noninvasive (antiarrhythmic drugs, medical therapy for heart failure, programming of implantable devices) therapies is commonly required. The aim of this review is to present the available therapeutic options, with main focus on recently published data for catheter ablation and provide a stepwise treatment approach.

Keywords: Ventricular arrhythmias, severe heart failure, ventricular tachycardia ablation, ICD programming

Introduction

Severe heart failure (s-HF) is the end stage of heart failure (HF) spectrum, when symptoms become refractory to medical therapy and optimal medical therapy (OMT) is poorly tolerated due to hemodynamic instability [1]. Ventricular arrhythmias (VAs) are commonly encountered in this population. VAs in the clinical context of s-HF are an indicator of adverse prognosis and they further deteriorate the ventricular function leading to unexpected hospitalizations due to electrical storms and decompensations [2]. In this review, the term VAs will refer to sustained ventricular tachycardia (SVT), frequent non-sustained ventricular tachycardia (NSVT) and frequent premature ventricular contractions (PVCs).

Adverse ventricular remodeling in HF can be highly arrhythmogenic. Dispersion of ventricular repolarization due to damaged cell membranes with impaired ion handling, in combination with the increased sympathetic tone are among the triggers. In addition, fibrotic areas serve as substrate for reentry circuits [3, 4]. Management of VAs in this population requires individualization according to the type of the arrhythmia (monomorphic or polymorphic) and the primary cause of HF.

Treatment includes invasive and noninvasive options. Antiarrhythmic drugs (AADs) can be used as initial therapy in cases of life-threatening VAs. However, no AAD have shown decrease in all-cause mortality while their proarrhythmic effects and side effects are non-negligible. Invasive suppression of the arrhythmic burden with catheter ablation (CA) has emerged as an effective therapeutic option. One year arrhythmia recurrence rate has been reported between 23% and 49% after CA in patients with ischemic HF. Clinical outcomes are inferior for non-ischemic myocardial substrate [5]. Timing of CA as well as the severity of HF seems to be among the prognostic factors. Pre-procedural

planning is essential for patients with s-HF, since short term mechanical hemodynamic support (MHS) may be needed.

This review aims to: i) summarize the existing knowledge regarding the invasive and noninvasive management of VAs in s-HF with emphasis on the latest published trials for ventricular tachycardia ablation and the optimal ICD programming; and ii) suggest a stepwise treatment approach for VAs management in s-HF.

Electrophysiological changes in HF

In healthy ventricular cardiomyocytes the action potential starts in phase 0 with the opening of sodium channels (rapid depolarization - I_{na} current). By the end of this first phase the cell membrane has reached its peak voltage value. Phase 1 follows, as depolarization activates voltage-gated potassium channels, leading to an outward potassium current (early repolarization, calcium independent transient outward potassium current I_{to1}). In phase 2, the plateau phase, the leakage of potassium continues by the delayed rectifier potassium channels (I_{KS}) while calcium enters the cell through L-type calcium channels. The accumulation of calcium intracellularly activates an additional current of calcium from the sarcoplasmic reticulum (SR) to cytoplasm fired by calcium binding to ryanodine receptors (RyRs). Phase 3 starts with the closure of L-type calcium channels while the outward current of potassium augments by the function of both slow and rapid delayed rectifier potassium channels (I_{Ks} and I_{Kr}). During this phase, another potassium current starts in the opposite direction, the inwardly rectifying potassium current (I_{K1}). This inward movement of potassium serves in restoring ion balance of the cell (in combination with pumps and exchangers e.g., sodium-potassium pump, calcium exchanger) in the last phase of the action potential, the phase 4 [6].

Arrhythmogenesis in HF patients starts in intracellular level due to changes in action potential features. Starting from phase 1, the under expression of the outward potassium current I_{to1}, encoded by Kv4.3 gene, prolongs the early repolarization phase leading to prolongation of the action potential duration (APD). Cellular repolarization is additionally impaired by down-regulation of genes related to the inward movement of potassium - the inward rectifier potassium current (I_{K1}) - acting in phase 3, which favors early after depolarizations (EADs) to occur [7].

Apart from potassium, defective calcium homeostasis contributes to triggered activity by EADs and delayed after depolarizations (DADs). Activation of the multifunctional calcium/calmodulin-dependent protein kinase II (CaMKII), a protein abundant in myocardial muscle cells, is enhanced in HF patients. CaMKII phosphorylates and promotes the activity of target membrane proteins leading to increased rapid influx of sodium in phase 0 (I_{na} current), prolonged influx of calcium in phase 2 - through L-type calcium channels - and increased leakage of calcium from sarcoplasmic reticulum, by activating ryanodine receptors (RyRs) [8]. Areas of damaged myocardial cells with impaired handling of calcium, exhibit abnormal contractions. During these contractions, calcium is released out of the cells from the injured cellular membrane. Extracellular increase in regional calcium creates arrhythmogenic contractile waves that propagates to nearby cells leading to PVCs and arrhythmogenesis through triggered activity [9].

The aforementioned alterations do not equally affect all myocardial muscle layers. Heterogeneity in electrophysiological properties exists throughout the myocardial wall, with epicardial layers being affected the least and endocardial layers the most [10, 11]. Intracellular communication is further impaired by dysfunctional gap junctions leading to cell-to-cell uncoupling [12]. In patients with s-HF, gap junction remodeling involves down-regulation of connexin43, reduction in gap junction plaque size and increased diversity of gap junction distribution [13]. As a consequence, the electrical impulse does not conduct uniformly in the ventricles. Abnormal wavefronts that propagate through cells of diverse electrophysiological properties can fire VAs [7, 14] (**Figure 1**).

Medical therapy of ventricular arrhythmias

Landmark studies for the prevention of SCD in HF have established the superiority of ICDs over medical therapy [15-18]. In the meantime, no AAD has been related to a reduction in all-cause mortality in the clinical context of HF, with the exception of beta-blockers. The main role of AADs in patients with HF and ICDs is to

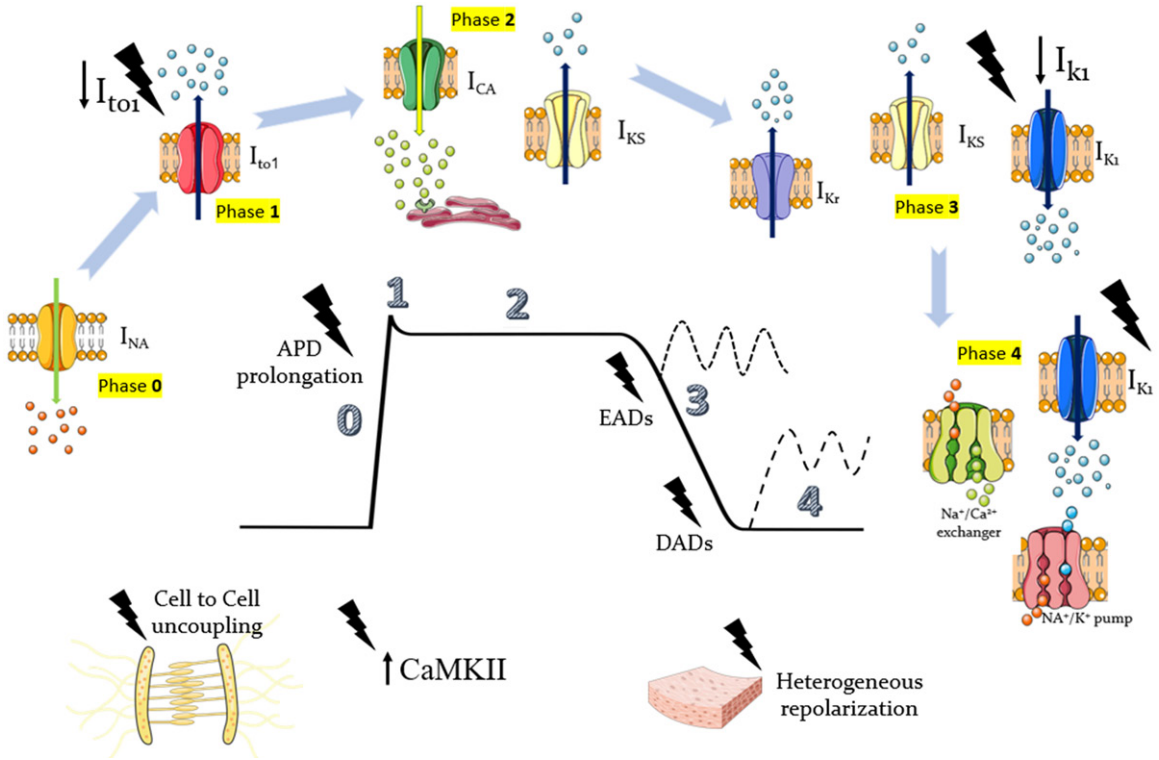

Figure 1. Arrhythmogenesis in heart failure is multifactorial. Early repolarization is affected by the downregulation of the I_{to1} current leading to prolonged action potential duration. Cellular repolarization is additionally impaired by downregulation of genes encoding the inward rectifier potassium current I_{K1}. Early and delayed afterdepolarizations are triggered by defective calcium and potassium homeostasis. Repolarization changes do not equally affect all myocardial layers leading to transmural heterogeneity. I_{na}: sodium current, I_{to1}: transient outward potassium current, I_{ca}: calcium current through L-type calcium channels, I_{ks}: delayed rectifier potassium channel (slow), I_{kr}: rapid delayed rectifier potassium channel, I_{k1}: inwardly rectifying potassium channel, CaMKII: calcium/calmodulin-dependent protein kinase II, APD: action potential duration, EADs: early afterdepolarizations, DADs: delayed afterdepolarizations.

reduce ICD therapies which affect both the quality of life of the patients and limit the longevity of the device [19]. Patients with ICD for secondary prevention of SCD or a history of ICD shocks are more likely to need additional therapy with AADs during their follow-ups [20]. The major drawback of AADs is related to their safety, especially in the clinical context of HF. Negative inotropic effect, toxicity, drug to drug interactions and proarrhythmic effects limit their utility in clinical practice [21, 22]. An acceptable strategy is to initiate AAD therapy immediately after the first appropriate shock has been delivered, closely monitor for side effects and reduce gradually the dose, provided that the clinical status of the patient is stabilized.

Choices for AADs in HF patients are very limited. As reported in the CAST trial, category Ic is hazardous for patients with ischemic cardiomyopathy (ICM), especially in the clinical setting of active ischemia [23]. Among sodium blocking agents, procainamide has proven superiority over amiodarone in terminating hemodynamically tolerated sustained monomorphic ventricular tachycardia (SMVT) of unknown etiology with less side-effects [24]. However, its use in patients with s-HF is not advised. Mexiletine, is usually combined with amiodarone for cases of refractory VAs or as an alternative when amiodarone toxicity has occurred [25]. Hypokalemia and hypomagnesemia should be corrected prior to its use and physicians should be aware of a possible hemodynamic deterioration in patients with s-HF due to increase in systematic vascular resistance [26]. Lidocaine, an intravenously administered Ib class agent, may be used in the acute setting of ischemic VT [27]. However, lidocaine is relative ineffective in terminating scar-related VTs [28].

Class II of AADs, beta-blockers, are part of the OMT in HF as they delay disease progression,

reduce all-cause mortality and prevent SCD [29]. Metroprolol, bisoprolol and carvedilol are the most well-established agents for use in patients with reduced ejection fraction [30-32]. As for their antiarrhythmic effects, beta-blockers are effective in suppressing ventricular ectopic beats due to the reduction of the sympathetic tone and the inhibition of the release of calcium waves that may occur spontaneously in a failing heart (as mentioned in the previous section) [33]. In cases of electrical storm, propranolol may be the beta-blocker of choice [34].

Amiodarone, the major AAD from class III, is the most widely acceptable choice for VAs suppression in the clinical setting of s-HF [35]. However, its extracardiac side-effects are non-negligible [36]. Except from potassium channels, amiodarone blocks sodium and calcium channels, beta-adrenoreceptors and directly reduces the sympathetic tone. Intravenous administration of amiodarone is useful for the acute termination of hemodynamically tolerated VT and as an adjuvant therapy in patients with ICDs to reduce arrhythmic burden and prevent shock therapies. In the OPTIC trial, the combination of beta-blockers with amiodarone was the most effective in reducing ICD therapies, in comparison to monotherapy with sotalol or beta-blockers [37]. In patients with structural heart disease (SHD) who experience recurrent, symptomatic SMVT or ICD shocks despite treatment with beta-blocker and amiodarone, beta blocker can be replaced by sotalol [38].

Beyond conventional AADs, the most recent additions to OMT in HF, sacubitril/valsartan and SGLT2 inhibitors have been associated with a reduced incidence of VAs, SCD and ICD interventions [39-42]. The mechanism of their antiarrhythmic action is not fully understood but is most likely related to the reverse remodeling of the ventricle [43]. Lastly, although research around inhibitors of CaMKII has been intensive (class IVe in a modernized classification of cardiac AADs), there are no clinically approved agents up to date [44-46].

Catheter ablation of ventricular arrhythmia

Catheter ablation strategy

CA is an invasive therapeutic option for the suppression of malignant VAs. For patients with s-HF, the risk from the procedure should be weighed against the possible benefits. CA for the suppression of electrical storm, unresponsive to conservative measures, is a challenging clinical scenario. SMVT is the most common arrhythmia related to electrical storms in patients with SHD [38]. Under these circumstances, the use of AADs may fail to terminate the tachycardia but rather increase its cycle length, leading to incessant forms of slow VT. CA is preferred over AADs escalation in this case. Except from electrical storm, CA is indicated for patients with HF and recurrent, symptomatic SMVT or ICD shocks for SMVT when chronic amiodarone therapy has failed [39]. Lastly, HF patients non respond to cardiac resynchronization therapy (CRT) due to frequent VAs (low biventricular pacing) should also be considered for CA [47].

The most common mechanism of arrhythmia in patients with HF and SMVT is reentry due to functional or anatomical block [48]. Hemodynamically tolerated tachycardias can be mapped and ablated using activation mapping and entrainment during the arrhythmia [49]. However, patients with impaired systolic function are unlikely to tolerate fast ventricular rates for the completion of the procedure. Substrate mapping techniques during sinus rhythm provide an alternative strategy for patients with HF and poorly tolerated VAs to undergo CA with less risk of hemodynamic deterioration. The most well-established techniques for substrate-guided ablation/modification are scar homogenization, scar dechanneling (homogenization with less extensive ablation), elimination of areas of local abnormal ventricular activities (LAVAs) and late potentials and lastly, targeting areas of local deceleration of propagation (isochronal crowding) [50-55]. However, the properties of the myocardial substrate can dynamically change during the arrhythmia, leading to alterations in the myocardial substrate that are not evident during mapping in sinus rhythm. For this reason, further diagnostic tools to perform functional substrate mapping are under development [56]. Epicardial substrate modification in addition to endocardial is warranted in a significant number of patients with s-HF [57] (**Figure 2**).

Even though substrate-guided ablation is a less aggressive strategy in comparison to activation mapping for patients with HF, CA is a procedure

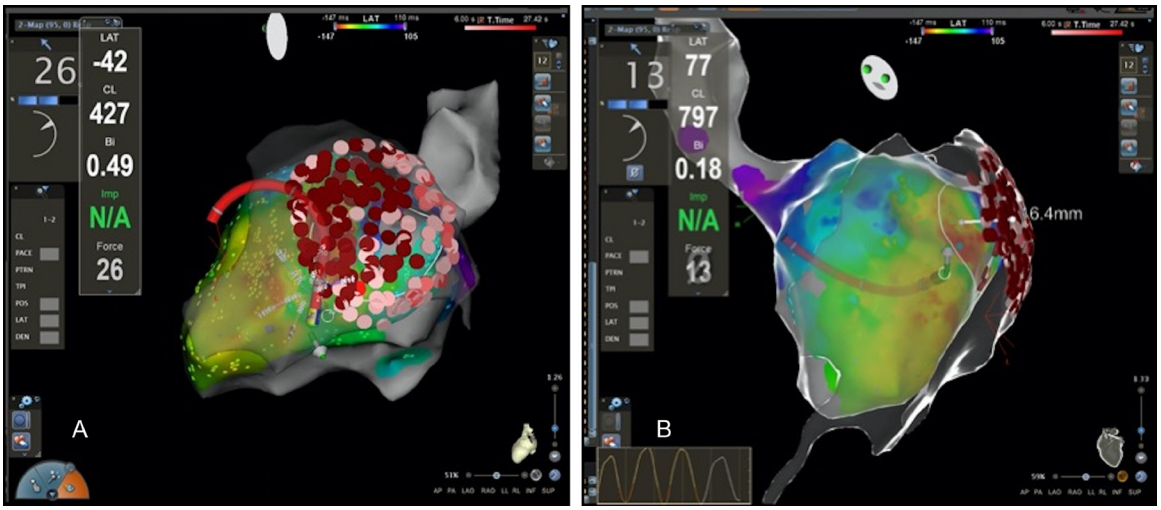

Figure 2. Combined epicardial (A) and endocardial (B) substrate modification in a patient with non-ischemic cardiomyopathy and electrical storm.

that can lead to hemodynamic decompensation especially for frail patients with s-HF. It requires prolonged time in supine position while the use of irrigated catheters increase the given amount of fluid. The PAAINESD score can be used pre-procedurally in order to identify high risk patients susceptible to acute hemodynamic deterioration [47]. High risk patients should be supported with short term MHS during CA.

Among the available choices for MHS, extracorporeal membrane oxygenation (ECMO) is the most compatible with electrophysiological procedures [58]. The cannulation is achieved by peripheral access allowing undisturbed mapping of the endo - or epicardial myocardial surface. The procedure can be prolonged and activation mapping can be achieved without hemodynamic compromise [59]. Incidence of acute death or decompensation is low under these circumstances of advanced MHS even for frail patients [60-62]. However, complications associated with the use of ECMO such as heparin induced thrombocytopenia, thromboembolism, vascular access complications and neurologic injury have been described [63, 64]. Regarding the other types of temporary MHS, intra-Aortic Balloon Pump Counterpulsation (IABP) is of limited value because it requires stable cardiac rhythm that cannot be ensured during CA. As for the use of impella, apart from the increased cost, the motor of the device interferes with the electromagnetic field of the three-dimensional mapping system leading to inaccessible sites in the outflow area [65-67].

Optimal timing of catheter ablation

The decision to escalate management of VAs from non-invasive to invasive therapies requires expertise and individualization. Optimal timing of VT ablation for patients with HF remains questionable. Up to date, recent guidelines suggest CA to be performed immediately before or shortly after ICD implantation in patients who receive ICD for secondary prevention (IIB indication) [38].

Indeed, ICD implantation (for secondary prevention) in combination with CA was superior to ICD plus medical therapy in terms of ICD interventions, while no differences in cardiovascular hospitalization or mortality was observed in the PAUSE-SCD study [68]. The spectrum of SHD was wide in the cohort (34.7% ICM, 30.6% non-ischemic cardiomyopathy-NICM- and 34.7% arrhythmogenic right ventricular cardiomyopathy-ARVC) with mean LVEF of 40%. The performed CA technique was the extensive elimination of LAVAs and conduction zones with isochronal crowding during sinus rhythm. If the arrhythmia was hemodynamically tolerated, activation mapping and entrainment were also performed. Non-inducibility of the tachycardia at the end of CA was encouraged but not mandated as an optimal end point of the procedure.

Improvement in hard endpoints (death/worsening HF hospitalizations) may be demonstrated by applying stricter criteria in the selection of patients for CA. The recently published PARTITA trial used a mixed population of both ICM and NICM and offered CA in the second phase of the trial, only to those who suffered an appropriate ICD shock due to VT unresponsive to ATP (11% of the initial cohort). 47 patients were included in the invasive arm (primarily with ICM-81%) with an average LVEF of 32.2%. The preferred CA strategy was the complete elimination of LAVAs in sinus rhythm. Epicardial approach was performed, whenever needed. The acute endpoint of the ablation was the complete elimination of LAVAs, which was confirmed with remapping and VT non-inducibility with a complete stimulation protocol. After a follow up of 24 months, early invasive strategy with VT ablation within two months after the first ICD shock reduced the composite endpoint of death or worsening HF hospitalization (95% of the patients in the ablation arm compared with 57% of patients in the control arm) while recurrent arrhythmic episode treated with shock were limited (9% in the ablation group versus 42% in the control group) [69]. Limitations of the study are the low number of participants and the increased number of non-cardiac deaths in the ablation arm.

The superiority of VT ablation in HF has also been demonstrated over the escalation of AADs. As confirmed by the results of the SURVIVE-VT and the previously published VANISH study [70, 71], the benefit toward CA was mainly driven by the increased incidence of complications related to AADs in the conservative groups. Therapy with AADs is not as benign as it is thought. Apart from well-known side effect, AADs can increase hospitalizations and worsen HF by increasing the cycle length (CL) of VT to heart rates below therapeutic zones of ICDs, leading to incessant slow VT or by causing bradycardia and increase in ventricular pacing with possible deleterious effects in the ventricular function.

ICD programming

Clinical significance of ICD shocks in HF

Optimal ICD programming is crucial for the prevention of inappropriate and unnecessary shocks in ICD recipients. The term inappropriate shock has been introduced for the delivery of therapy for non-ventricular tachyarrhythmias while the term unnecessary or avoidable shock refers to hemodynamically tolerated VTs terminated by shock therapy, which would have otherwise resolved spontaneously or would have responded to ATP therapy [72]. ICD shocks in patients with HF have been associated with an increased risk of mortality [17, 73-75]. It is unclear whether the reason of the deterioration is the defibrillation itself (myocardial injury, myocardial stunning) [76] or if the malignant arrhythmogenesis which caused the activation of the ICD indicate an already deteriorating myocardial substrate. The increase in the mortality risk has been reported for both appropriate and inappropriate shocks, even though appropriate shocks may carry the worst prognosis (5-fold increase in the risk of the death after an appropriate shock in comparison to a 2-fold increase of mortality risk after an inappropriate shock in the SCD-HeFT trial) [17, 73, 74].

Only the delivery of the first appropriate shock was associated with an increased mortality risk in a recent analysis which combined data from five significant trials in the domain (MADIT II, MADIT-Risk, MADIT-CRT, MADIT-RIT, RAID). Subsequent shocks did not further worsen the prognosis, with the exception of electrical storm. The major determinant of mortality after ICD shock was the underlying myocardial substrate, while ICD therapies for fast VT (exceeding 200 beats per minute) were associated with the highest risk of subsequent death (HR: all > 2.8; $P < 0.001$) [77]. On the contrary, appropriate therapy for VT less than 200 bpm or inappropriate shocks did not reach statistically significant increase in mortality. As a conclusion, life threatening VTs (fast sustained VT/VF) may serve as prognostic markers of HF deterioration and death. ICD appropriate activation in HF patients should raise awareness in clinical practice for a subsequent clinical deterioration while treatments that modify the myocardial substrate, as CA, may be protective [78].

ICD programming to prevent unnecessary therapies

Even though the true contribution of the shock in the mortality is inconsistent between studies, avoidance of painful unnecessary ICD

shocks protects the quality of life of the patient and limit the occurrence of post-traumatic stress disorder [79, 80]. Six landmark studies in the field of device programming (MADIT-RIT, ADVANCE III, EMPIRIC, PROVIDE, PREPARE and RELEVANT) concluded that reserving ICD therapies only for high rate ventricular tachyarrhythmias and/or using longer detection intervals are safe strategies that limit both appropriate and inappropriate shocks [81-86]. For instance, in MADIT-RIT trial the high-rate therapy group (HR ≥ 200 bpm, delay 2.5 sec) and the delayed therapy group (three zones - HR between 170-199 bpm and delay 60 sec, HR between 200-249 bpm and delay 12 sec and HR ≥ 250 bpm and delay 2.5 sec) experienced less frequently the study endpoints (time to first occurrence of inappropriate shock and all-cause mortality) in comparison to the conventional group (two zones - HR between 170-199 bpm and delay 2.5 sec, HR ≥ 200 bpm and delay 1 sec) [81]. During 15 months follow up of the same cohort, the delayed and high-rate strategies were still superior over the conventional programming even after the first episode of sustained VT (HR ≥ 170 bpm for at least 30 sec) or after receiving their first ICD therapy for a high-rate VT (HR ≥ 200 bpm) in terms of reducing the risk of both appropriate and inappropriate shocks [87]. According to a meta-analysis, these strategies may have the potential to reduce all-cause mortality by 30%, a trend driven by the avoidance of inappropriate shocks [88, 89].

ICD programming differs between primary and secondary prevention ICD recipients. In the first case, little is known about the characteristics of future VAs while in the second case, the tachycardia zone should be adjusted to include the rate of the clinical tachycardia. It is recommended to program the slowest tachycardia therapy zone limit ≥ 188 bpm in primary prevention ICD patients [38].

In all cases, ATP is the recommended first line therapy for all VT zones with a rate up to 230 bpm with the exception of cases where ATP has been documented to be ineffective or proarrhythmic in past therapies. At least one attempt of ATP should be programmed with a minimum of 8 stimuli at a cycle length of 84-88% of the tachycardia cycle length (T-CL) [90]. Burst at CL close to 88% of the T-CL is preferred over Ramp for fast VTs while ATP cycle length between 75-84% of T-CL may be attempted for slower VTs [91, 92]. ATP is expected to have a success rate of up to 90% in terminating slow VTs (HR between 188-200 bpm) with a 1-5% risk of acceleration [83]. Addition of a second attempt of ATP for hemodynamically tolerated VTs may increase the effectiveness of the therapy [90]. ATP may be individualized by observing the return cycle of the clinical tachycardia after unsuccessful ATP. ATP that manages to reset the T-CL without terminating it has successfully entered the circuit but has not achieved bidirectional block. Adding an extra-stimulus after the burst train may lead to termination. On the other hand, in cases where the ATP did not affect the T-CL at all, adding more stimuli to the burst train may help the penetration of the pacing wavefront to the tachycardia circuit by 'peeling back refractoriness' [93] (**Figure 3**). Regarding shock therapies, in most cases they should be programmed after the ATP failure and the maximum available energy is preferred especially in the high-rate zone to increase the success rate of the defibrillation [90]. Low-energy shocks carry the risk of accelerating VT to VF. In addition, in case of inappropriate shock due to rapidly conducting atrial fibrillation, high energy shocks are more likely to terminate it and avoid subsequent inappropriate shocks [93].

Invasive reduction of sympathetic tone in refractory cases

Invasive elimination of the sympathetic tone through cardiac sympathetic denervation (CSD) and renal denervation (RDN) is a last resort therapy for refractory cases. CSD can be achieved temporarily, through percutaneous injection of an anesthetic agent into the thoracic epidural space, a technique mainly used for hemodynamically unstable patients in VT storm unresponsive to conventional therapy or permanently as an elective procedure performed by video-assisted thoracoscopic surgery (resection of the lower half of the stellate ganglion and the second through fourth thoracic paravertebral ganglia) [94, 95]. In a cohort of 68 patients with mean LVEF of 32%±13%, ICM or NICM and recurrence of scar-mediated monomorphic VT after CA, CSD significantly reduced the expected risk of recurrences and limited ICD shocks [96]. Similarly, RDN, a therapy primarily developed for patients with refrac-

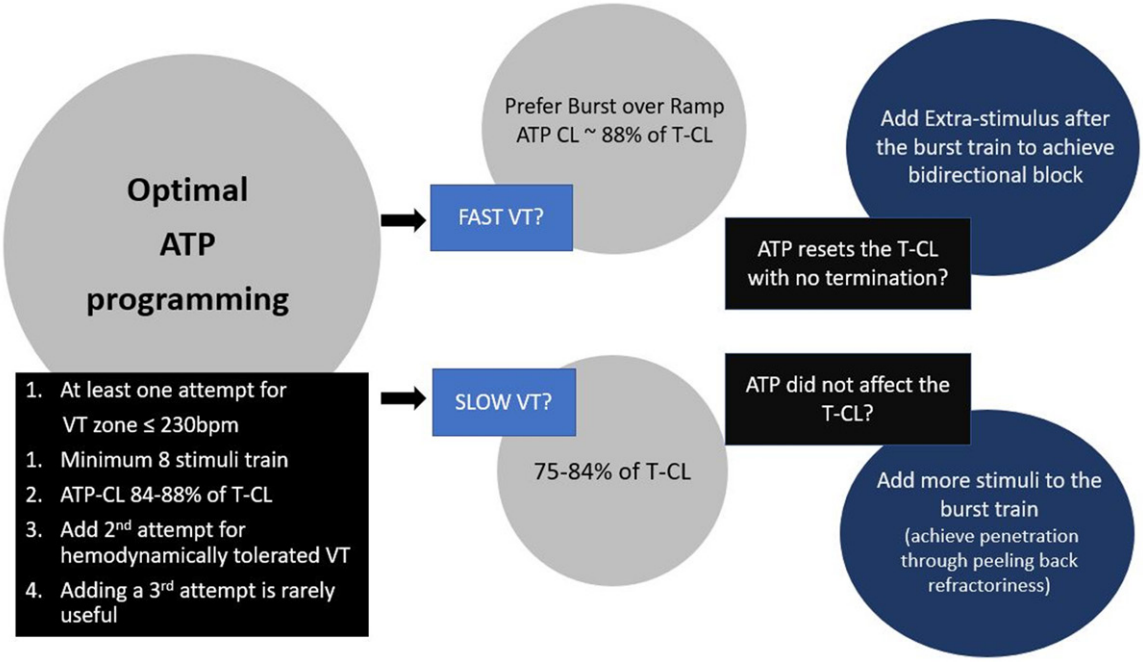

Figure 3. Optimal strategy for antitachycardia pacing (ATP) programming. T-CL: tachycardia cycle length, CL: cycle length.

tory arterial hypertension, has been associated in small studies with a reduction in the arrhythmic burden of patients with cardiomyopathies and refractory ventricular arrhythmias [97-99]. RDN can be combined with CSD as an adjunctive therapy for high-risk patients [100].

A stepwise approach for the management of patients with s-HF and VAs

Patients with s-HF are in risk of SCD and carry a strong indication for ICD implantation. Most of the times, these patients have received an ICD for primary or secondary prevention in a prior stage of the disease. The main question that needs to be answered in the evaluation of a patient with s-HF and documented VAs is the necessity of providing therapy. Therapy should be provided in patients who are symptomatic, have a high burden of VAs (> 10-20% PVCs), suffer recurrent appropriate ICD shocks, have experienced electrical storm or have failed to improve with resynchronization therapy due to high burden of PVCs. Before starting antiarrhythmic treatment, the physician should ensure that the patient is receiving the maximum tolerated dose of all categories of OMT for HF. Reversible causes should be excluded (ischemia, electrolyte imbalance, fluid retention, infection, thyroid dysfunction) and the ICD should be optimally programmed to provide shocks only for necessary therapies and prefer ATP over shock whenever feasible.

The addition of amiodarone and an increase or a switch of the beta-blocker are usually the first steps for the reduction of the arrhythmic burden and the patient should be evaluated for CA. CA should always be considered after the first delivery of appropriate shock or at the time of ICD implantation when the ICD is implanted for secondary prevention (as suggested by PARTITA and PAUSE-SCD trials). Monomorphic VT or a high burden of a monomorphic PVC are the most suitable VAs for CA. CA should be performed in specialized, highly experienced centers with availability of MHS.

Pre-procedural evaluation for short term MHS is crucial for patients with s-HF. If the risk of decompensation is high, short term MHS should be offered or the necessity of the procedure should be reconsidered. As for the ablation strategy (substrate mapping/activation mapping, epicardial or endocardial approach) and the desired endpoints (complete elimination of LAVAs, non-inducibility of the arrhythmia), they should be priorly defined in order to

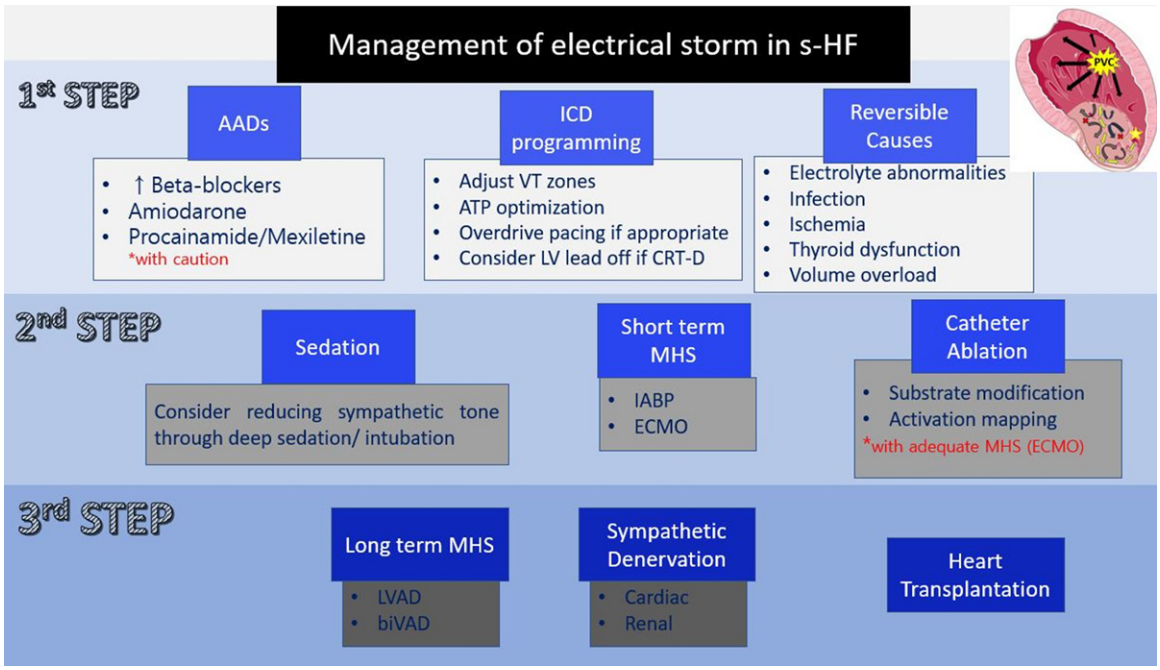

Figure 4. Management of electrical storm in severe heart failure. S-HF: severe heart failure, AADs: Antiarrhythmic drugs, VT: ventricular tachycardia, ATP: antitachycardia pacing, LV: left ventricle, CRT-D: cardiac resynchronization therapy-defibrillator, MHS: mechanical hemodynamic support, IABP: intra-aortic balloon pump, ECMO: extracorporeal membrane oxygenation, LVAD: left ventricular assist device, biVAD: biventricular assist device.

ensure proper preparation of both the patient and the team and avoid unnecessary delays.

Invasive reduction of the sympathetic tone with CSD and RDN may be offered (according to availability). If CA fails to improve the arrhythmic status of the patient or if the arrhythmia is not suitable for CA (polymorphic VT, VF). In cases of electrical storm, apart from escalation of AADs and CA, sedation/deep sedation and short or long term MHS are additional therapeutic measures (**Figure 4**).

Lastly, sudden deterioration of the arrhythmic status of a previously stable patient with s-HF should always raise awareness of a deteriorating myocardial substrate or an imminent decompensation. Subsequently, early evaluation for escalation of hemodynamic support (long term MHS, intermittent use of inotropes) or increased priority for heart transplantation should be ensured.

Conclusions

Malignant arrhythmogenesis is common among patients with end stage HF leading to SCD, frequent hospitalizations, triggering decompensations and painful ICD therapies. VAs and HF constitute a vicious cycle as the abnormal myocardial substrate generates and preserves abnormal arrhythmic wavefronts and sustained VAs further deteriorate the systolic function of the ventricle. Management of VAs in this population is challenging. Optimal ICD programming is crucial for the prevention of unnecessary therapies. Limited options exist regarding pharmacological depression with AADs, mainly due to proarrhythmic and negative inotropic effects. CA can provide an effective invasive therapy for the reduction of the arrhythmic burden leading to less ICD therapies and as a bail out option in patients with electrical storm. Careful pre-procedural planning is essential for the safety of the procedure. Short term MHS may be needed because of the frailty of this population. Invasive reduction of the sympathetic tone with CSD and RDN is an additional therapeutic option reserved for refractory high-risk cases.

Acknowledgements

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Disclosure of conflict of interest

None.

Abbreviations

ATP, anti-tachycardia pacing; CL, cycle length; CSD, cardiac sympathetic denervation; HF, heart failure; ICD, Implantable cardioverter defibrillator; LVEF, left ventricular ejection fraction; MHS, mechanical hemodynamic support; OMT, optimal medical therapy; RDN, renal denervation; s-HF, severe heart failure; SMVT, sustained monomorphic ventricular tachycardia; T-CL, tachycardia cycle length; Vas, ventricular arrhythmias.

Address correspondence to: Dr. Konstantinos P Letsas, Arrhythmia Unit, Onassis Cardiac Surgery Center, Athens 17674, Greece. E-mail: k.letsas@gmail.com; letsas@ocsc.gr

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