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MANAGEMENT OF VENTRICULAR TACHYCARDIA IN HEART FAILURE

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Abstract

Ventricular tachyarrhythmias are common in patients with congestive heart failure. The clinical presentation ranges from an asymptomatic incidental electrocardiographic finding to palpitations, syncope, and sudden cardiac death. Although implantable cardioverter defibrillators successfully prevent sudden cardiac death associated with ventricular fibrillation and ventricular tachycardia, recurrent implantable cardioverter defibrillators shocks remain a clinical management challenge. In this review, we discuss management strategies of ventricular tachycardia in congestive heart failure, including drug therapy, radiofrequency catheter ablation (RFCA), and recent RFCA advances.

Background

Ventricular tachycardia (VT) is common in patients with heart failure (HF).[1-3] It is a significant cause of mortality as sustained VT can degenerate into ventricular fibrillation (VF) and cause sudden cardiac death (SCD). Implantable cardioverter defibrillators (ICDs) have shown to prevent SCD in patients with HF and are the mainstay of both primary and secondary prevention therapies.[4-6] ICDs, however, can be an adverse psychological burden on patients.[7] Repeated shocks pose a significant clinical challenge due to pain and hemodynamic deterioration, and they are associated with increased mortality.[8] Furthermore, ICDs do not provide absolute protection against SCD. In one study, the rate of SCD in patients with ICD devices was 5%.[9]

The limitations of ICDs create clinical scenarios in which patients require specific treatments to minimize the occurrence of VT/VF and recurrent ICD shocks. It is reasonable for clinicians to adopt alternate strategies to minimize VT/VF occurrence in this high-risk population so that ICDs serve solely as a backup. One such strategy is the use of antiarrhythmic drugs (AADs), which have been tested for prophylaxis and therapy against VT in multiple studies; however, the results have mostly been disappointing. Radiofrequency catheter ablation (RFCA) is another option that has shown promise in recent trials.[10, 11] RFCA uses thermal energy to ablate the myocardium that serves as substrate for re-entrant VT circuits. Recent advances in three-dimensional (3D) electroanatomical mapping systems enable reconstruction of VT circuit pathways during sinus rhythm, allowing RFCA in patients with unmappable VTs.[12]

Despite the efficacy of RFCA in treating recurrent VTs in most patients, there remains a small group of patients for whom RFCA is unsuccessful. In such patients, coronary ethanol ablation has shown to be effective if the site of VT origination is mapped near a coronary artery or vein branch.[13, 14] This review discusses the aforementioned advances in prophylaxis and treatment of VT in patients with heart failure.

Antiarrhythmic Drug Therapy

Over the past few decades, multiple risk markers for SCD have been used to design AAD trials in patients with coronary artery disease (CAD), nonischemic cardiomyopathy, and congestive heart failure (CHF). These include frequent premature ventricular contractions (PVCs), complex PVCs, ventricular couplets, nonsustained VT (NSVT), reduced left-ventricular ejection fraction (LVEF), and advanced HF. Several randomized clinical trials have assessed the efficacy of AADs for preventing SCD when used alone (Table 1).[6, 15-31]

According to multiple large clinical trials, ICD therapy is indicated and is superior to AADs in patients with advanced HF (LVEF ≤35%) or recurrent VTs.[4-6] In many patients with ICDs, however, adjuvant AAD therapy also is initiated to reduce ICD therapies. For example, in the device arm of the Antiarrhythmics versus Implantable Defibrillators (AVID) trial,[32] about 18% of patients had to be started on adjuvant AAD therapy to reduce multiple shock occurrences and prevent recurrent ventricular arrhythmias. It is suggested that AADs prolong the tachycardia cycle, therefore making it more amenable to antitachycardia therapy. Also, by reducing the number of shocks, AADs can improve the device's battery life.

AADs are of particular importance in the management of electrical storms. Prompt hospitalization to reverse the precipitating factors and acute administration of AADs is indicated in these cases to ensure survival.[33] However, in patients who present with electrical storms while on AADs, acute intravenous AAD therapy will likely fail. In these cases, the patient will require emergent catheter ablation.[34, 35] Table 2 summarizes the major clinical trials concerning the use of adjuvant AAD therapy in patients with an ICD.[36-42]

There are multiple drawbacks to using AADs either as standalone or adjuvant therapy. First, most AADs are poorly tolerated by patients. In the Optimal Pharmacological Therapy in Cardioverter Defibrillator Patients (OPTIC) trial, the rate of drug discontinuation at 1 year was 23.5% for patients taking sotalol and 18.2% for those taking amiodarone. Drug toxicity is another concern in patients taking AADs. For example, long-term use of amiodarone is associated with significant pulmonary and thyroid toxicity.[43] AADs also can increase mortality through a net proarrhythmic effect.[16, 17] Futhermore, they also may interfere with ICD function by altering the defibrillation and pacing thresholds.[44] Based on these drawbacks, AADs do not seem to be an effective long-term option and therefore should be used with extreme caution, especially in patients with significant structural heart disease.

Drugs	Study	Inclusion Criteria	Endpoints	Drugs	Control	Key Results
Class I	CASH[15]	Recent cardiac arrest not associated with MI	Total mortality Arrhythmic death	Propafenone Metoprolol Amiodarone	ICD	Sudden cardiac death mortality lowest in the ICD arm; increased mortality in the propafenone arm
	CAST[16, 17]	Post-MI ≥6 PVCs/hr LVEF ≤40%	Arrhythmic death	Flecainide Encainide Moricizine	Placebo	Arrhythmic death increased in all treatment arms
	IMPACT[18]	Post-MI	Rate of PVCs and complex ventricular arrhythmias Mortality	Mexiletine	Placebo	Rate of PVCs and complex ventricular arrhythmias was lower in treatment arm at 4 months and a trend towards reduction was observed in treatment arm at 12 months; trend towards mortality increase in treatment arm
Class II	BHAT[19]	Post-MI	Total mortality Sudden cardiac death	Propranolol	Placebo	Total mortality and sudden cardiac death decreased in treatment arm
	CAPRICORN[20]	Post-MI LVEF ≤40%	Death or arrhythmias	Carvedilol	Placebo	Death or arrhythmia decreased in carvedilol arms; ventricular arrhythmias also decreased in treatment arm
	CIBIS-II[21]	NYHA Class III-IV LVEF ≤35%	All-cause mortality	Bisoprolol	Placebo	All-cause mortality was less in treatment arm; rate of sudden cardiac death less in treatment arm
	MERIT-HF[22]	NYHA Class II-IV LVEF ≤40%	All-cause death Sudden cardiac death	Metoprolol CR/XL	Placebo	All-cause death and sudden cardiac death lower in treatment arm
Class III	ANDROMEDA[23]	NYHA Class III-IV LVEF ≤35%	Death from any cause or hospitalization for HF Arrhythmic death	Dronedarone	Placebo	Increased mortality as well as arrhythmic death in treatment arm
	BASIS[24]	Post-MI PVCs	Total mortality Arrhythmic events	Amiodarone	Placebo	Total mortality and arrhythmic events lower in treatment arm
	CAMIAT[25]	Post-MI ≥10 PVCs/hr or NSVT	Arrhythmic death Total mortality	Amiodarone	Placebo	Amiodarone reduced arrhythmic death but did not reduce total mortality
	CHF-STAT[26]	CHF LVEF ≤40% ≥10 PVCs/hr	Total mortality	Amiodarone	Placebo	No effect in ischemic cardiomyopathy but there was a trend towards mortality reduction in nonischemic cardiomyopathy
	DIAMOND-MI[27]	Post-MI (≤7 days) LVEF ≤35%	All-cause mortality Arrhythmic death	Dofetilide	Placebo	No reduction of all-cause mortality or arrhythmic death in treatment arm
	EMIAT[28]	Post-MI LVEF ≤40%	Total mortality Arrhythmic death	Amiodarone	Placebo	Amiodarone reduced arrhythmic death but did not reduce total mortality
	GESICA[29]	CHF LVEF ≤35%	Total mortality	Amiodarone	Best therapy	Amiodarone reduced total mortality; patients with NSVT had higher mortality
	MUSTT[30]	Post-MI LVEF ≤30% NSVT	Arrhythmic death or cardiac arrest	ICD Class I or class III agents	No therapy	Improved survival in ICD group; no difference between antiarrhythmic therapy and no therapy
	SCD-HeFT[6]	CHF LVEF ≤35% NYHA II-III	Total mortality Arrhythmic death Cost Quality of life	ICD Amiodarone	Placebo	Improved survival with ICD; no effect of amiodarone on survival
	SWORD[31]	Post-MI LVEF <40% *or* Remote MI NYHA Class II-III	Total mortality	*d*-Sotalol	Placebo	Increased mortality in treatment arm

Table 1. List of major randomized clinical trials involving antiarrhythmic drugs and their effect on mortality and sudden arrhythmic death. MI: myocardial infarction; ICD: implantable cardioverter defibrillator; PVC: premature ventricular contraction; LVEF: left ventricular ejection fraction; NSVT: nonsustained ventricular tachycardia; CHF: congestive heart failure; NYHA Class: New York Heart Association heart failure class.

Study	Inclusion Criteria	Endpoints	Drugs	Control	Key Results
Pacifico et al.[36]	History of VTs ICD with shocks	All-cause death or all-cause ICD shock Mean frequency of shocks	Sotalol	Placebo	Sotalol decreased all-cause death or all-cause ICD shocks; sotalol also decreased mean frequency of shocks
Kuhlkamp et al.[37]	Sustained VT or VF Inducible VT or VF	Recurrence of VT or VF Total mortality	Sotalol Sotalol/ICD	Placebo ICD only	Patients with inducible VT/VF after treatment with sotolol received ICD; sotalol decreased incidence of VT/VF recurrence; total mortality was unchanged across all arms
Seidl et al.[38]	Indication for ICD	Appropriate ICD therapy by ATP or shock Actuarial survival rate	Metoprolol	Sotalol	Appropriate ICD therapy was lower in metoprolol group; actuarial survival rate was not significantly different
Kettering et al.[39]	Sustained VT or VF ICD	Recurrent VT or VF requiring ICD therapy Event-free survival Total mortality	Metoprolol	Sotalol	The rate of VT/VF recurrence, event-free survival, and total mortality between the treatment arms was not statistically significant
Singer et al.[40]	ICD Inducible VT At least one shock in prior year	Frequency of appropriate ICD shocks and ATP	Azimilide	Placebo	Frequency of ICD shocks and ATP was reduced in the treatment arm
SHIELD[41]	ICD VT or VF	All-cause shock and ATP All-cause shock Appropriate ICD therapy	Azimilide	Placebo	All-cause shock and ATP was reduced in the treatment arm; all-cause shock trend toward reduction in treatment arm; appropriate ICD therapy was reduced in treatment arm
OPTIC[42]	ICDVT or VF LVEF ≤40%	All-cause ICD shock Rate of drug discontinuation	Amiodarone + Beta-blocker	Beta-blocker Sotalol	All-cause ICD shock was lower in amiodarone + beta-blocker group compared to sotolol alone and beta-blocker alone; rate of drug discontinuation was highest for sotolol followed by amiodarone and lowest for beta-blocker

Table 2. List of major randomized clinical trials involving adjuvant antiarrhythmic drug therapy in patients with an ICD. VT: ventricular tachycardia; VF: ventricular fibrillation; ICD: implantable cardioverter defibrillator; ATP: antitachycardia pacing; LVEF: left ventricular ejection fraction.

Radiofrequency Catheter Ablation

RFCA is a potentially curative standalone therapy in patients with idiopathic VT due to its high success rate. However, its use in patients with structural heart disease is less straightforward. In these patients, RFCA often is used as an adjunctive therapy to ICDs in order to prevent or reduce the number of ICD shocks. This strategy has become attractive since AADs are not highly effective and are poorly tolerated.

The initial success of RFCA was limited to patients with stable VTs who could tolerate RFCA during VT induction in the laboratory from a hemodynamic standpoint. The introduction of electroanatomical mapping systems (EMS) has allowed RFCA, using substrate mapping, in patients with hemodynamically nontolerated or noninducible VTs.[45] EMS allows the creation of a 3D ventricular voltage map during sinus or paced rhythm. The map displays, in the 3D geometry of the left ventricle, color-coded amplitudes of the local bipolar electrical signals. Scars from previous myocardial infarction of other nonischemic infiltrative processes can be readily identified by the low amplitude of the local electrical signals (typically less than 1.5 mV).[45] This map displays low-voltage areas of scarring as well as regions with late potentials within the scars. Late potentials correspond to areas of slow conduction, in which (during sinus rhythm) activations reach these sites after the QRS. These sites serve as potential reentry circuits, and ablating them can effectively interrupt VT induction (Figure 1).[46] The development of irrigated electrodes that cool the electrode-tissue ablation interface allows radiofrequency delivery to deeper endocardial tissue, further facilitating RFCA of large VT circuits.[47] Catheter stability and precision of radiofrequency delivery is further improved with the use of Sensei® X Robotic Catheter System (Hansen Medical, Inc., Mountain View, CA).[48] Multiple clinical trials have demonstrated RFCA to be an effective therapy for VTs — either prophylactically at the time of ICD implantation or in patients with frequent ICD interventions.

Prophylactic RFCA therapy for ICD shock prevention has been assessed in two large clinical trials. The Substrate Mapping and Ablation in Sinus Rhythm to Halt Ventricular Tachycardia (SMASH-VT) multicenter trial enrolled patients with a history of MI who were either undergoing ICD implantation or had an ICD implanted within 6 months prior to enrollment. The indication for ICD implantation included VF, hemodynamically unstable VT, or syncope with inducible VT during electrophysiological testing.[10] Patients also were enrolled if they had their ICDs implanted for primary prevention and subsequently received appropriate shock therapy for a single event. In the ablation arm, there was a 65% reduction in ICD therapies (shocks and antitachycardia pacing) during the 2 years of follow up ($P = 0.007$). When antitachycardia pacing was excluded, the patients with ablation had a 73% ($P = 0.003$) reduction in the risk of receiving an ICD shock therapy. A trend towards fewer deaths during follow-up was also observed

in patients within the ablation arm. The second trial, Ventricular Tachycardia Ablation in Coronary Heart Disease (VTACH), enrolled patients who had an indication for ICD for secondary prevention after stable irreversible VT, coronary artery disease, previous MI, or reduced LVEF (≤50%).[11] These patients received RFCA using electroanatomical substrate mapping prior to ICD implantation. The primary endpoint of this trial was time to first VT or VF recurrence. Patients were followed for a mean of 22.5 months. Time to recurrence of first VT or VF event was 18.6 months in the ablation group compared to 5.9 months in the control group. At 2 years, the estimate of survival free from VT or VF was 47% in the ablation arm and 29% in the control arm (P = 0.045). ICD shocks occurred in 32.7% of the ablation group at 2 years follow-up compared to 53.7% of the control group. The incidence of ablation-related death was 0% in both trials, and the rate of major complications was 4.7% and 3.8%, respectively. In light of these two studies, RFCA is recommended in patients with an ICD device and multiple ICD therapies.

Two large prospective trials have evaluated the use of RFCA in patients with ICD who had experienced multiple shock deliveries or incessant VTs and had failed AAD therapy.

The Cooled RF Ablation System clinical trial enrolled 146 patients who had hemodynamically stable VTs but had failed at least two AAD therapies.[49] The patients were randomized to either RFCA or continuation of AADs. Of these patients, 79% either had

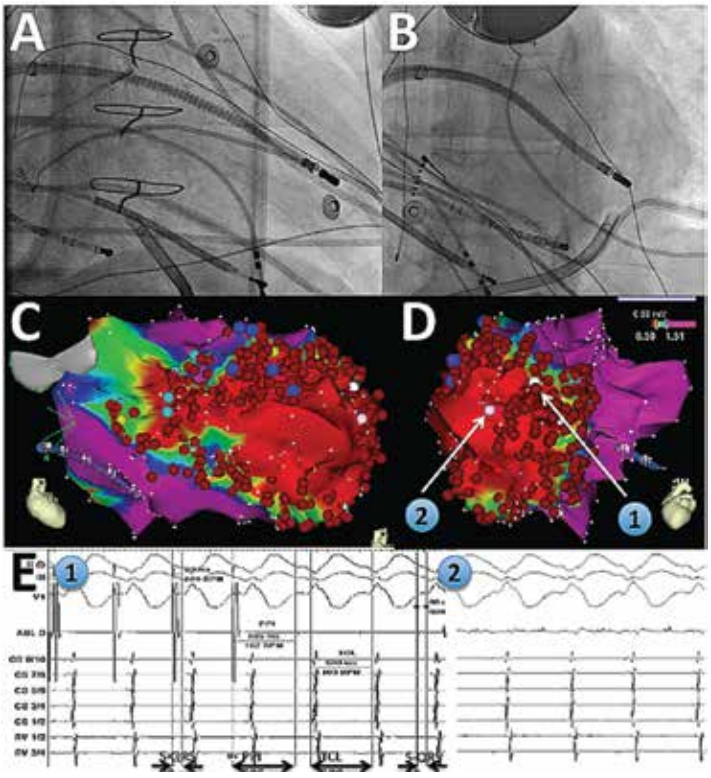

Figure 1. Catheter ablation of ventricular tachycardia using a robotic system. A and B show right anterior oblique and left anterior oblique fluoroscopic views of the robotic catheter system reaching the LV apex (in particular, the lateral aspect of the apex) where the LV VT substrate was found. An epicardial sheath is also present. C and D show corresponding 3D maps of bipolar endocardial voltage amplitudes, demonstrating a large scar (red). Sites 1 and 2 correspond to the exit site of the VT circuit and its mid-diastolic location, respectively. E1 on the left shows pacing from site 1, with concealed entrainment and post-pacing interval (PPI) identical to the VT cycle length (TCL), and stimulus-to-QRS delay identical to signal-to-QRS (S-QRS). E2 on the right shows a mid-diastolic potential at site 2 during VT.

LV: left ventricular; VT: ventricular tachycardia.

an ICD at the time of enrollment or had one implanted prior to discharge. The mean number of VT episodes within the preceding 2 months was 25 ± 31. Acute termination of all mappable VTs was achieved in 75% of patients, while 41% of patients had acute termination of all VT types. Clinical success, defined as ≥75% reduction of VT frequency at the 2-month follow-up, was observed in 81% of the patients. One or more episodes of VT occurred in 46% of patients, with a median time to first VT episode of 24 days. The Kaplan-Meier recurrence rate of VT was 56% at 1 year. The rate of major complications related to RFCA was 8%, and the mortality rate at 1-year follow-up was 25%.

The Multicenter Thermocool VT Ablation Trial was a larger multicenter study with 231 patients. In contrast to the Cooled RF trial, this trial included patients with both mappable and unmappable VTs. Of these patients, 37% had a previous RFCA procedure, 70% had failed AAD therapy with amiodarone, and 94% had an ICD at the time of enrollment. A median of 11 VT episodes was recorded in each patient in the preceding 6 months, and 16% of patients had incessant VTs. The primary endpoint of freedom from recurrent incessant VTs at the 6-month follow-up was achieved in 53% of the patients. The median of VT episodes was reduced from 11.5 to 0 at the 6-month follow-up compared to the 6-month period preceding RFCA. While 20% of patients had an increase in their VT episodes, 67% had a ≥75% reduction of VT episodes. The procedure mortality rate was 3% and the 1-year rate was 18%.

RFCA of VTs is effective in patients with HF and ICD both prophylactically and after multiple shocks. RFCA also is indicated acutely in patients with an electrical storm that is not responsive to intravenous AADs. Finally, RFCA is indicated in patients with incessant VTs that are slow and not detected by ICD. It is important to recognize that AADs are often continued in patients after RFCA. SMASH-VT is the only trial in which AAD therapy was stopped in patients following ablation. A direct comparison of optimal AAD therapy versus RFCA is being evaluated in the VT Ablation Versus Enhanced Drug Therapy (VANISH) trial that is currently in the enrollment phase.

Coronary Alcohol Ablation

Although RFCA with or without AAD therapy has proven effective for suppression of recurrent VTs, some patients have recurrent episodes and require repeat ablations.[50] Some patients, however, remain refractory to multiple RFCAs and AAD therapy. These patients tend to have VTs with deep intramural circuits that an ablation catheter cannot access. In such cases, coronary ethanol ablation has shown great promise. In this method, ethanol is injected into a coronary artery branch proximal to the VT circuit. Since ethanol can penetrate into the myocardial tissue, it can ablate deeper circuits that are inaccessible to RFCA.

In a recent study, 27 consecutive patients with recurrent VTs and failed RFCA were considered for coronary artery alcohol ablation. Of these, 22 patients had a VT circuit that was mapped proximal to a coronary artery branch.[51] Alcohol ablation successfully terminated the targeted VT in 82% of the patients. Recurrence of VT was observed in 14 (64%) of patients within a median of 16 days. However, 8 of these 14 patients had a VT storm or incessant VTs, and 6 of them remained free of these conditions. Therefore, coronary artery ethanol ablation successfully terminated or improved VTs in 63.6% of the patients. A complete heart block occurred in 5 patients (22.3%), and 3 patients (13.6%) with advanced HF died within 30 days of the operation.

We recently presented two cases in which a retrograde transcoronary venous approach was attempted for delivery of alcohol to the myocardium. Both patients had incessant VTs

and had failed multiple RFCA attempts and AADs. Successful termination of all inducible VTs was achieved in both patients without any periprocedural complications.[14]

Alcohol ablation is a reasonable "last resort" for patients with incessant VTs or electrical storms who remain refractory to AAD and RFCA therapies. Major limitations of this procedure are unpredictability of alcohol delivery and risk of vascular and tissue damage in unwarranted regions.

Conclusion

In the past few decades, antiarrhythmic drug therapy has been widely used for suppression of ventricular arrhythmias in patients with heart failure. These drugs, however, are very poorly tolerated by patients due to their toxic side effects. Radiofrequency catheter ablation is a better option for prevention and suppression of ventricular arrhythmias in HF patients, and it has a very high safety margin. Coronary artery or venous ablations are reasonable in patients with refractory VTs who have failed previous RFCA attempts. However, they carry higher complication rates and are limited to a few large academic centers with very experienced clinicians.

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