Current Management of Ventricular Tachycardia: Approaches and Timing

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Abstract

Ventricular tachycardia (VT) in the presence of structural heart disease is associated with sudden cardiac death and warrants prompt attention. Implantable cardioverter defibrillators (ICDs) while highly effective in terminating sustained ventricular arrhythmias and reducing mortality, have no effect on the arrhythmia substrate and recurrent shocks for VT termination occur in approximately 20% of patients. Shocks worsen quality of life and are associated with progression of heart failure and increased mortality. Antiarrhythmic drugs, mainly in the form of beta-blockers or amiodarone, are moderately effective in reducing ICD therapies but drug intolerance and serious toxicities of amiodarone necessitate drug cessation in a quarter of patients. Catheter ablation has emerged as an effective treatment for control of frequent VT episodes and can be life saving in cases of incessant VT or VT storm. As experience increases, it is being used increasingly earlier, rather than a last resort therapy. Efficacy varies with the nature of the underlying heart disease. Intramural arrhythmia substrate and failure to create permanent ablation lesions remain challenges and repeat procedures are necessary in a third to a half of patients. For idiopathic VTs or PVCs that are symptomatic or worsen LV function, catheter ablation is often an effective therapy.

Keywords: ventricular tachycardia; ablation; idiopathic ventricular tachycardia; polymorphic ventricular tachycardia

Introduction

Ventricular tachycardia (VT) can be monomorphic, with each QRS the same as the preceding and following QRS, or polymorphic, with a continually changing QRS. The latter, when sustained, usually results in syncope or cardiac arrest. Sustained monomorphic VT (SMVT) may be hemodynamically stable or unstable based on the rate of the tachycardia, underlying ventricular function and volume status of the patient. Thus the arrhythmia can have various manifestations. In patients with structural heart disease SMVT is associated with a risk of sudden death as the arrhythmia can degenerate to ventricular fibrillation. Alternatively, VT may cause syncope, or, if the rate of the VT is slow, patients may present with progressive heart failure. The most common presentation now is in patients who will have received an implanted cardioverter defibrillator (ICD) due to prior VT or a known risk for sudden death. These patients present with repeated ICD therapies due to VT. The term “VT storm” describes three or more episodes of VT that occur within a 24-hour period and warrants immediate attention as it is associated with a high mortality [1, 2].

A small proportion of SMVT is due to idiopathic VT, occurring in patients with no identifiable structural heart disease. Patients with idiopathic VT generally have a good prognosis and sudden death is rare [3]. Thus, they are managed differently from
those with structural heart disease. The distinction between VT associated with structural heart disease and idiopathic VT is therefore crucial in formulating management strategies. This review will focus on recognition of VT mechanisms, current therapeutic options and timing of interventions such as catheter ablation in the management of VT.

**Types of VTs and Related Mechanisms**

The approach and outcomes of treatment are dependent on the nature of the arrhythmia substrate. The presenting arrhythmia often suggests the arrhythmia mechanism and location of the arrhythmia substrate. Monomorphic PVCs or VT have the same ventricular activation sequence from beat to beat. The QRS morphology is a clue to its origin. The majority of sustained monomorphic VTs (MVT) is due to scar related re-entry. The scars can remodel over time producing recurrent VT after years of stability. A single large ventricular scar can support multiple VT circuits, causing VTs with different QRS morphologies and rates. Once VT occurs, up to 40–50% of patients will experience a recurrence within 2 years [4].

In approximately 8–10% of patients, MVT originates from the Purkinje system due to automaticity or re-entry [5]. A specific form of VT due to bundle branch reentry is seen typically in patients with structural heart disease, and inter-ventricular conduction delay or left bundle branch block on the sinus rhythm ECG. The re-entry wavefront propagates antegrade down the right bundle, then through the septum and retrogradely up the left bundle to complete the reentrant circuit. VT has a left bundle branch block-like configuration, but the circuit can also revolve in the reverse direction, creating a VT with right bundle branch block pattern. Although catheter ablation of the right bundle is curative, most patients have other scar-related VTs as well [6].

Idiopathic VT often manifests as monomorphic PVCs or repetitive MVT and most commonly has a focal origin. These VTs are typically provoked by adrenergic stimulation and triggered automaticity is the likely mechanism. The right and left ventricular outflow tracts are the most common origins followed by regions adjacent to an AV valve annulus or within a papillary muscle [3]. Frequent idiopathic PVCs and repetitive VT may lead to LV dysfunction. However, it can be difficult to know if the arrhythmia is idiopathic and causing ventricular dysfunction, or is a consequence of ventricular disease. A specific form of idiopathic LV VT due to re-entry within the fascicles is responsive to verapamil (Belhassen’s VT) and amenable to catheter ablation.

Polymorphic VT is characterized by beat-to-beat variation in QRS morphology due to varying ventricular activation sequences and frequently degenerates into ventricular fibrillation. These arrhythmias are usually triggered by acute myocardial ischemia, electrolyte disturbances, or repolarization abnormalities such as QT prolongation induced by drugs (e.g. class 3 antiarrhythmic drugs), hypokalemia, chronic bradycardia and combinations of these factors. Polymorphic VTs are also encountered in ventricular hypertrophy and heart failure. Patchy areas of myocardial fibrosis, common in the non-ischemic cardiomyopathies, can theoretically predispose to spiral wave break up of a re-entrant VT producing a polymorphic VT.

Rarely, monomorphic PVCs of Purkinje origin can trigger ventricular fibrillation (VF) often presenting with electrical storms. Although initially described in patients without structural heart disease and termed “idiopathic VF”, it is recognized that PVC triggered VF can also occur in patients with heart failure, prior myocardial infarction, and cardiomyopathies, including amyloidosis [7, 8].

**Management of Ventricular Tachycardia**

Initial management after termination of the acute arrhythmia is directed toward identification of structural heart disease and exclusion of potential predisposing factors such as electrolyte abnormalities and myocardial ischemia. When a patient with no prior known cardiac history presents with a sustained VT, coronary angiography, and echocardiography are common early investigative steps. Cardiac magnetic resonance imaging with gadolinium contrast injection is helpful in defining ventricular morphology, function and the presence of myocardial scarring,
infiltration or inflammation, which may help clinch specific diagnoses such as arrhythmogenic RV cardiomyopathy and amyloidosis [9].

VT storm that is hemodynamically unstable and fails to be suppressed by beta-blockers, amiodarone and lidocaine may warrant deep sedation including the use of general anesthesia to reduce sympathetic drive. Inability to control unstable VT should prompt consideration of ventricular assist devices and urgent catheter ablation in an experienced center (see below).

Unless a reversible cause is identified, a sustained ventricular tachycardia in association with structural heart disease usually warrants consideration of implantable cardioverter defibrillator (ICD) placement (Figure 1).

**Implantable Cardioverter Defibrillators (ICDs)**

ICDs are highly effective for termination of ventricular fibrillation or tachycardia and improve mortality in cardiac arrest survivors and in patients at risk for sudden death due to structural heart diseases [10]. In all cases ICDs are recommended only if there is also expectation for survival of at least a year with acceptable functional capacity (Figure 1). The exception is in cases of patients with end-stage heart disease who are awaiting cardiac transplantation outside the hospital, or who have left bundle branch block QRS prolongation such that they are likely to have improvement in ventricular function with cardiac re-synchronization therapy from a biventricular ICD.

Despite the high efficacy of ICDs for termination of ventricular arrhythmias, there is considerable morbidity associated with their use. ICD shocks are painful, associated with increased mortality, mostly from deteriorating heart failure and may result in post traumatic stress disorder [11]. Inappropriate or unnecessary shocks due to sinus tachycardia, atrial fibrillation, non-sustained VT or lead malfunction occur at an annual rate of approximately 3.5% [12]. In addition, unnecessary right ventricular pacing can aggravate ventricular dysfunction from pacing induced dys-synchrony and should be avoided [13]. Appropriate programming of ICD arrhythmia detection criteria and anti-tachycardia pacing therapy to terminate VT can reduce the odds of necessary and unnecessary shocks without compromising safety [14].

ICD implantation has a 3% risk of complications, including pneumothorax, cardiac perforation, bleeding, and heart failure decompensation, but the procedure related mortality is less than 1% [15]. ICD infections require device and lead removal,
with a 0.25% procedural mortality in experienced centers. Patients receiving ICDs require careful follow-up to detect arrhythmias that are predictive of heart failure deterioration and monitoring for device malfunction, and assessment of battery life. Remote monitoring systems that allow automated and patient triggered transmissions of ICD recordings has simplified follow-up and enhanced early detection of arrhythmias and ICD problems [16].

**Drug Therapy for Ventricular Arrhythmias**

Drugs have an important role in reducing the frequency of recurrent symptomatic arrhythmias. Beta-adrenergic blockers are the most commonly used drugs because many arrhythmias are provoked by sympathetic stimulation, and they have a favorable safety profile [10]. However, they have limited efficacy for suppressing re-entrant arrhythmias associated with structural heart disease.

Membrane active antiarrhythmic drugs that block cardiac ion channels have little role in preventing sudden death in patients with structural heart disease, but are useful for reducing symptomatic arrhythmias. The sodium channel blocking drugs such as flecainide and propafenone are occasionally considered for idiopathic VTs, but these agents should be avoided in patients with heart disease. They have negative inotropic effects, and flecainide increased mortality when given to survivors of myocardial infarction [10]. Quinidine is better tolerated hemodynamically due to its effect on action potential duration and its vasodilatory properties that tend to offset any negative inotropy from sodium channel blockade. However, all these drugs have significant proarrhythmic effects such that use of sodium channel blockers in patients with structural heart disease is largely limited to those with an ICD. Drugs that predominantly block potassium channels (sotalol, dofetilide) prolong repolarization and are better tolerated in patients with structural heart disease. However, these drugs can cause torsade de pointes VT, and the risk is likely increased in heart failure due to electrophysiologic changes that accompany myocardial hypertrophy and impaired excretion of many drugs. Careful monitoring for excessive QT prolongation during initiation is required.

Both oral amiodarone and sotalol reduce ventricular and atrial arrhythmias that can lead to ICD shocks [17]. Amiodarone is most effective for control of ventricular arrhythmias but extra-cardiac toxicities (prominently thyroid, lung, liver, and neurologic) prevent long-term use in more than 20% of patients. In a recent trial in patients with LVEF $\leq$ 35%, amiodarone had no effect on mortality in NYHA class II heart failure, but was associated with increased mortality in class III heart failure [18]. Nevertheless, amiodarone is a reasonable consideration for patients who have had spontaneous sustained VT or VF, but who have a contraindication to or refuse to have an ICD. Newer antiarrhythmic drugs including analogues of amiodarone such as dronadarone, have been disappointing because of limited efficacy and increased mortality in patients with heart failure [19].

**Catheter Ablation for Ventricular Arrhythmias**

**General Considerations**

Catheter ablation has emerged as an important therapeutic option for most ventricular arrhythmias. Recent advances in imaging, ablation techniques and hemodynamic support have allowed for safe and effective ablation even in unstable patients. Hence, ablation should be an early consideration in the course of recurrent VT that trigger symptoms or ICD shocks. However, patient selection should consider careful balancing of risks and benefits. Appropriate expertise and facilities including cardiac surgical back up is needed for optimal success while minimizing procedural risks [6].

Prior to endocardial ablation, ventricular thrombus should be excluded by echocardiography in patients with structural heart disease. The presence of concomitant atrial fibrillation without a sufficient period (>4 consecutive weeks) of therapeutic anticoagulation, must prompt consideration of transesophageal echocardiogram to exclude a left atrial appendage thrombus, as cardioversion of VT during ablation may revert the patient to sinus rhythm with heightened risk of thromboembolism. General anesthesia is increasingly used in our laboratory during ablations for scar-related VT. It has the advantage of keeping the patient still dur-
ing long procedures, which facilitates the use of electro-anatomic mapping systems and is preferred when pericardial access is necessary for epicardial mapping and ablation [20].

Hemodynamic support using percutaneous Left Ventricular Assist Devices (pLVAD) with an Impella Recover 2.5 (Abiomed, Inc.), a Tandem Heart Device (CardiacAssist, Inc.) or extracorporeal membrane oxygenators (ECMO) may be considered for selected high risk patients to allow extended mapping during VT. Recent small retrospective series have shown that pLVAD support is feasible during ablation [21]. VTs could be mapped for relatively longer periods of time and were terminated by RFA more often compared to historical control groups without hemodynamic support or with an intra-aortic balloon pump. However there was no difference in acute procedural success or VT recurrence rates during follow up. In addition the magnetic motor of the Impella system can interfere with electroanatomic mapping systems, especially during mapping in the ventricular outflow tracts. Extracorporeal membrane oxygenation (ECMO) offers biventricular support and does not interfere with the mapping systems. ECMO does not unload the LV as compared to pLVAD but offers better hemodynamic support (4–6 L/min).

As most patients with heart disease undergoing ablation have an ICD, the majority of VTs are documented on intracardiac electrograms (EGMs) recorded from the pacing and defibrillating electrodes rather than a 12-lead electrocardiogram. These EGMs can provide clues to the nature of the arrhythmia and their assessment is important to exclude the possibility of unnecessary ICD therapy due to atrial fibrillation or sinus tachycardia at rates above the VT detection rate. Long-short intervals from some pacing algorithms, such as the minimal ventricular pacing mode, initiate VT in some patients and can be corrected by reprogramming. The presence of a uniform PVC initiating VF can be a clue to triggers from the Purkinje fibers [8]. Intracardiac EGMs also allow documentation of the VT cycle length and the response to anti-tachycardia pacing that may be helpful in assessing the nature of the arrhythmia.

Whenever possible, a 12 lead ECG recording of spontaneous VT (termed a clinical VT) should be obtained as the QRS morphology suggests the VT origin, which facilitates planning of the initial mapping approach. A right bundle branch block-like configuration in lead V1 indicates likely LV origin, and a left bundle branch block-like configuration indicates a septal or RV origin. Superior and inferior frontal plane axes indicate exit from the inferior or anterior walls respectively. Dominant R or S waves in V3/V4 indicate a basal or apical origin respectively. These guidelines are not always reliable, particularly in the presence of extensive scars. In non-ischemic cardiomyopathy, QS complexes in lead I during VT often indicates that VT arises from a circuit in the sub-epicardium of the basal lateral LV. These criteria are not reliable in ischemic heart disease [6, 22, 23].

**Approaches to Ablation in Structural Heart Disease**

Programmed ventricular stimulation should be performed first to induce the arrhythmias to unequivocally confirm the diagnosis, assess the QRS morphology, and define an endpoint for ablation. If non-inducible or the induced arrhythmia is hemodynamically unstable, a substrate based mapping and ablation approach is generally used. If the VT is inducible and hemodynamically tolerated, the reentrant circuits can be characterized using mapping techniques and ablation applied to terminate VT, providing confirmation that the ablation target is causing the VT.

In substrate-based approaches to mapping and ablation, scar regions are defined during sinus or paced rhythm by creating voltage maps of the area of interest. There is a close correlation of endocardial and epicardial scar with low EGM voltage (bipolar EGM less than 1.5 mV on the endocardium and 1.0 mV for the epicardium) [24]. Endocardial bipolar EGMs do not reliably identify intramural or epicardial scar, but these can often be detected from analysis of unfiltered or minimally filtered unipolar EGMs, as these have a broader “field of view” [22, 23, 25].

In addition to defining the area of low voltage, specific features of recorded EGMs allow definition of the reentry substrate. Multicomponent, fractionated EGMs, split or late potentials (occurring after the QRS complex) indicate asynchronus activation of myocyte bundles with intervening fibrosis causing
slow conduction [18, 26, 27]. Pacing in the area of interest identifies excitable tissue in the scar, areas of slow conduction characterized by long stimulus to QRS intervals, and a paced QRS morphology that approximates the morphology of the VT suggests close proximity to the VT circuit exit. Ablation is performed during stable sinus or paced rhythm, targeting these abnormal areas. Our approach is to render the tissue electrically un-excitable to pacing to attempt to insure that an adequate ablation lesion is created [28, 29].

In approximately 5–15% of patients with coronary artery disease, and more than a third of patients with non-ischemic cardiomyopathy, scar-related VT circuits are located in the sub-epicardium and cannot be ablated from the endocardium. In the absence of pericardial adhesions from prior cardiac surgery or pericarditis the epicardium can be accessed percutaneously for mapping and ablation. Epicardial ablation is usually preceded by coronary angiography to make sure a coronary vessel does not over lie the ablation target, with risk of coronary occlusion due to ablation [30, 31].

If a clinical VT, defined as one that has occurred spontaneously, is inducible at the beginning of the procedure, non-inducibility of such VT is the minimum procedural endpoint that is sought. Abolition of all inducible VTs has been associated with a lower risk of VT recurrence and cardiac mortality in some, but not all studies [32, 33]. Location of arrhythmia substrate (usually scar) and the underlying disease state affects the likelihood of success. Ablation is most successful in conditions where potential re-entry channels can be defined on the endocardium or epicardium (e.g. myocardial infarction, arrhythmogenic right ventricular cardiomyopathy) but is less successful for intramural circuits or epicardial circuits in close proximity to coronary arteries [34, 35]. Ablation failure is often due to inability to create transmural, durable lesions or failure to reach intramural substrate (e.g. intraventricular septum), or protection of the VT substrate by close proximity to coronary arteries or the left phrenic nerve, or by epicardial fat.

Transcoronary ethanol ablation has been used in selected patients when catheter ablation fails. A coronary vessel supplying the VT substrate is identified for administration of absolute ethanol. Limitations include failure to identify a coronary target, potential for damage to large areas of myocardium and administration of intravenous contrast load in HF patients who may have pre-existing renal impairment [36]. Surgical cryoablation is also an option when catheter ablation fails and may allow separation of an overlying coronary artery from epicardial substrate and dissection through epicardial fat allowing successful ablation [37].

**VT Ablation in Specific Substrates**

*Ischemic Cardiomyopathy*

Ventricular scar is present from prior myocardial infarction, with ongoing remodeling, creating the anatomic substrate for scar-related, often multiple, re-entrant VTs [6]. Challenges for post infarct VT ablation include: (i) inducibility of multiple VTs (on average 3/patient due to separate reentry circuits or a shared area of slow conduction with variable exits); (ii) likelihood of a broad reentry circuit isthmus (>2–3 cm) [38]; (iii) hemodynamically unstable VTs [6, 39]. Hence substrate mapping is increasingly preferred to mapping during VT.

Multicenter studies of catheter ablation in ischemic cardiomyopathy show that at least one VT is abolished in 72–96% of patients and all inducible VTs eliminated in 38–72% of patients with 50–88% of patients remaining VT free over a mean follow up of >12 months and 30–100% continuing on previously ineffective AADs [34, 40]. VT episodes are markedly reduced in the majority of patients [40]. Procedural mortality is approximately 3% with 1 year mortality of 9–18% with most deaths attributed to heart failure [6, 19, 40]. In prospective multicenter trials approximately 50% of patients have at least one recurrence of VT, but the frequency of VT episodes is reduced. Patients who fail ablation and have recurrent VT have a higher mortality than those who remain in sinus rhythm [41].

*Non-ischemic Cardiomyopathy*

Non-ischemic cardiomyopathy (NICM) is a heterogeneous group of diseases including idiopathic cardiomyopathy, genetic LV cardiomyopathies (lamin A/C, Titin mutations), arrhythmogenic RV cardiomyopathies (ARVC), inflammatory disease (sarcoid heart disease, myocarditis) and hypertrophic
cardiomyopathy (HCM). Sustained monomorphic VT is due to scar-mediated re-entry in over 80% of patients with the remainder being focal in origin or due to bundle branch re-entry. Key differences compared to ischemic cardiomyopathy include: (i) generally smaller scars with multiple re-entrant VTs despite small scar; (ii) predilection for anatomical location around the valve annuli or septum; (iii) less frequent transmural scars; (iv) more frequent intramural scars; (v) extensive epicardial scarring that may occur in the presence of normal endocardium or extend beyond the region of endocardial scarring [6, 42, 43]. A recent study found basal anteroseptal or inferolateral scar accounting for 89% of arrhythmogenic substrate in patients with NICM and sustained MVT [42]. The former can be targeted endocardially whereas the latter frequently require an epicardial approach.

Catheter ablation for VT in the non ischemic cardiomyopathies is less well studied and VT recurrence rates are higher than in the ischemic patients, occurring in 50–60% in short term follow up (up to 1 year), although VT burden can be significantly reduced. Complete non-inducibility can be achieved in 38–67% of patients [30, 42, 43].

In ARVC, fibrofatty replacement progresses from the subepicardial layer to the endocardium particularly affecting the free wall of the RV along the tricuspid annulus and in the outflow tract. Epicardial scar area is often larger than endocardial scar [44]. Thus epicardial ablation is frequently required either as a primary target or after failed endocardial ablation procedure [45]. With the use of epicardial ablation freedom from VT is achieved in 77–89% of patients, but late recurrences can occur due to the progressive nature of the disease [6, 44–46].

SMVT is rare in patients with HCM, and usually due to scar-mediated re-entry [38]. Combined epicardial and endocardial mapping and ablation is feasible and can reduce spontaneous VTs but data on outcome is limited [47, 48].

### Table 1

Indications for Catheter Ablation of Ventricular Tachycardia in Patients with Structural Heart Disease

(Adapted from Reference [6]).

<table>
<thead>
<tr>
<th>Catheter ablation of VT is recommended for</th>
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<tr>
<td>1. Patients with symptomatic sustained monomorphic VT (SMVT), including VT terminated by an ICD, that recurs despite antiarrhythmic drug therapy or when antiarrhythmic drugs are not tolerated or not desired;</td>
</tr>
<tr>
<td>2. Control of incessant SMVT or VT storm that is not due to a transient reversible cause;</td>
</tr>
<tr>
<td>3. Patients with frequent PVCs, NSVTs, or VT that is presumed to cause ventricular dysfunction;</td>
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<tr>
<td>4. Bundle branch reentrant or inter-fascicular VTs;</td>
</tr>
<tr>
<td>5. Recurrent sustained polymorphic VT and VF that is refractory to antiarrhythmic therapy when there is a suspected trigger that can be targeted for ablation.</td>
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<th>Catheter ablation should be considered for</th>
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<tr>
<td>1. Patients who have one or more episodes of SMVT despite therapy with one of more Class I or III antiarrhythmic drugs;</td>
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<tr>
<td>2. Patients with recurrent SMVT due to prior MI who have LV ejection fraction &gt;0.30 and expectation for 1 year of survival, and is an acceptable alternative to amiodarone therapy;</td>
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<tr>
<td>3. Patients with haemodynamically tolerated SMVT due to prior MI who have reasonably preserved LV ejection fraction (&gt;0.35) even if they have not failed antiarrhythmic drug therapy.</td>
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<th>VT catheter ablation is contra-indicated</th>
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<tr>
<td>1. In the presence of a mobile ventricular thrombus (epicardial ablation may be considered);</td>
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<tr>
<td>2. For asymptomatic PVCs and/or NSVT that are not suspected of causing or contributing to ventricular dysfunction;</td>
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<tr>
<td>3. When VT is due to transient, reversible causes, such as acute ischaemia, hyperkalaemia, or drug-induced torsade de pointes.</td>
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ICD, implantable cardioverter defibrillator; MI, myocardial infarction; VT, ventricular tachycardia; VF, ventricular fibrillation.
pharmacological options, in the hope of avoiding ICD shocks and antiarrhythmic drug toxicities. Table 1 summarizes current recommendations for the use of catheter ablation according to the 2009 EHRA/HRS Expert Consensus on Catheter Ablation of Ventricular Arrhythmias [6].

Two randomized trials (VTACH and SMASH-VT) explored the early (after the initial episode of VT) use of catheter ablation in ICD recipients with prior myocardial infarction, VT and impaired left ventricular (LV) function [4, 49]. Both studies found a significant reduction in VT recurrences during follow up of approximately 2 years. However, neither of these trials was sufficiently powered to examine mortality. In a retrospective study, Bunch et al. reported a lower risk of death and heart failure hospitalizations in patients treated with VT ablation after an ICD shock compared to patients managed medically only [50, 51]. Recent publications support an early invasive approach. In a single center, observational study, Dinov et al. reported better acute and long-term success if catheter ablation of scar-related VT was performed within 30 days after the first documented VT [34]. Once again, a mortality benefit was not evident in patients who underwent early VT ablation compared to those who had their ablation late (> 1 year) after their first presentation with VT. The benefits of early catheter ablation as compared to medical therapy are the subject of several ongoing randomized clinical trials.

**Management of VT Storm**

Electrical or VT storm is associated with a high mortality. A meta-analysis found a mortality of 17% during a little over 1 year follow up with heart failure accounting for ~2/3rd of all deaths [1]. Catheter ablation controls VT in >90% of patients with 74–92% remaining free of incessant VT or recurrent VT storm [1, 39]. Single episodes of VT recurrences occur in a third of patients [6]. Sympathetic denervation or renal artery denervation are emerging potential therapies [52]. In rare patients, recurrent VT is provoked by unifocal PVCs from the Purkinje fibers, outflow tracts, or papillary muscles that can be targeted for ablation (see above) [7, 8].

**Idiopathic PVCs or VT**

Idiopathic VT is a diagnosis of exclusion and often require the use of sophisticated imaging techniques such as cardiac MRI or positron emission tomography to exclude areas of scar or inflammation that may not be evident by echocardiography. Most idiopathic PVCs originate from the ventricular outflow tracts and tend to be monomorphic [3]. In some patients the arrhythmia arises from an extension of myocardium for a variable distance above the aortic or pulmonic valves. An autopsy study showed that extensions are most common in the right coronary cusp (55%) than the left coronary cusp (24%) and non-coronary cusp (<1%). In contrast, myocardial extensions above the pulmonic valves are evenly distributed (45–60%) [53]. Other sites for idiopathic PVCs include the papillary muscles, myocardium adjacent to the AV valves, and from the fascicles of the conduction system. An epicardial peri-venous focus has been identified in some patients and may need mapping in the great cardiac vein or the anterior inter-ventricular vein [54].

Very frequent PVCs or non-sustained VT can induce a cardiomyopathy that can be reversed with either pharmacological suppression or catheter ablation [55–57]. Such arrhythmias may also exacerbate pre-existing left ventricular function and is a cause of loss of effective biventricular pacing in patients dependent on cardiac re-synchronization therapy [58]. The diagnosis of PVC-induced cardiomyopathy is one of exclusion and often retrospective based on recovery of LV function after control of the arrhythmia.

The exact mechanism of PVC-induced cardiomyopathy is unclear. Ventricular dyssynchrony, alterations in intracellular calcium handling, changes in heart rate dynamics, hemodynamic parameters as well as changes in myocardial and peripheral autonomic function have been postulated [59]. The frequency of PVCs correlates with the severity of left ventricular dysfunction at the time of initial presentation [55, 56]. However, in some patients, a high PVC burden does not impair LV function whereas in others a lower PVC burden may do so. The lowest PVC burden resulting in a reversible cardiomyopathy was noted to be 10% in one study [55]. This relationship is likely to be complex however, not appreciated by
a single “cut off” value. PVC frequency can also vary substantially from day to day. PVC duration (≥140 ms to 150 ms), an epicardial site of origin, PVC coupling intervals ≤ 600 ms, PVC interpolation, a long history of palpitations (>60 months), and the complete absence of symptoms have all been associated with higher likelihood of LV dysfunction [59–63].

Beta-blockers and calcium channel blockers have only a modest effect in suppressing PVCs, but are commonly used for idiopathic PVCs because of their safety. More potent antiarrhythmic drugs such as flecainide, mexilitine and amiodarone are more effective but long term use is limited by side effects and flecainide is avoided in the presence of heart disease or depressed ventricular function [64]. Hence, catheter ablation is an attractive option for many patients. A recent randomized study of patients with frequent PVCs from the RV outflow tract found a greater decrease in burden of PVCs following ablation compared to drug therapy although LV function improved in both groups [65]. Whether PVC ablation is superior to drugs in reversing LV dysfunction is unknown.

The ECG can help localize site of arrhythmia origin. Most PVCs or VTs having a left bundle branch morphology with precordial transition at V3 and inferiorly directed axis, have a RV outflow tract origin. A prominent R wave in V1 or early transition before V3 with inferior axis suggests a left ventricular outflow tract origin. However, the complex anatomy of the outflow tract and variable distance of myocardial extensions above the valves precludes precise localization from ECG criteria [53]. Systematic mapping of the RV outflow tract pulmonary artery, great cardiac/anterior inter-ventricular vein via the coronary sinus followed by the aortic root and cusps, and LV outflow tract is often required. Papillary muscle VTs tend to have a broader QRS (typically greater than 150 milliseconds), usually have a monophasic R or qR in V1, and Q waves tend to be absent. The frontal plane axis is superiorly directed for those originating from the posterior LV papillary muscle and inferiorly directed when the origin is the anterior papillary muscle [66].

Catheter ablation is successful in achieving greater than 80% reduction in ectopic activity in 70–90% of patients, with highest success rates for arrhythmias arising from the RV outflow tract [57–59, 65]. The efficacy of ablation for the less common foci such as the LV outflow tract, are not well characterized. A common reason for failure is the inability to induce the arrhythmia for adequate mapping.

There is limited data on the time course of recovery of LV function after ablation of PVCs. One study showed that 68% of patients recover within 4 months with 32% requiring mean of 12±9 months (range 5–45 months) for recovery [60]. Early improvement (within 1 week) predicted near complete reversibility [67].

In patients with heart disease PVCs may be idiopathic or related to an abnormal substrate, such as within an infarct scar or at its border, and the site of origin may also correspond to the exit site of an inducible reentrant VT [68].

**Conclusion and Take Home Message**

Ventricular arrhythmias are an important cause of morbidity and mortality in patients with structural heart disease.

AADs are limited in their efficacy and catheter ablation has emerged as a useful therapy. HF remains the major cause of mortality after VT ablation, consistent with the concern that VT is an indication of disease progression in patients with impaired ventricular function, warranting attention to heart failure therapies.

The efficacy of catheter ablation for monomorphic VT varies with the underlying disease etiology, the pattern and distribution of scar, proximity of scar to critical epicardial structures and accessibility of scar areas for catheter ablation.

Novel technologies are hoped to improve future outcomes.

PVC-induced cardiomyopathy is important to recognize as a reversible condition. Further work is needed to elucidate the mechanism of PVC-induced cardiomyopathy and the relationship between PVC burden and development of cardiomyopathy.

**Conflict of Interest**

The authors declare no conflict of interest.
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