GORDON K. MOE LECTURE

Current treatment of ventricular arrhythmias: State of the art

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Ventricular arrhythmias may be benign, requiring only evaluation for associated risks and then reassurance, or associated with a risk of sudden death or significant morbidity. Therapies for these arrhythmias have evolved considerably over the past 20 years. For some, a definitive, curative therapy is available in the form of catheter ablation. Others are best managed with an implantable cardioverter-defibrillator that provides effective arrhythmia termination and protection from sudden death, with antiarrhythmic drugs or ablation to control recurrent arrhythmias. Although progress has been substantial, many challenges remain.

KEYWORDS Ventricular tachycardia; Ablation; Implantable cardioverter-defibrillator; Antiarrhythmic drug

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Introduction

Therapy for ventricular arrhythmias is guided by the estimated risk of sudden death posed by the arrhythmia, the likelihood of recurrence, symptoms, and the risks and benefits of therapies. Associated underlying heart disease and nature of the arrhythmia substrate are important considerations and is often suggested by the electrocardiographic (ECG) characteristics of the arrhythmia (Figure 1).

Monomorphic ventricular tachycardia (VT) has the same ventricular activation sequence from beat to beat, producing similar QRS complexes from beat to beat. The QRS morphology is often a good indication of the site of initial ventricular activation, and hence the location of the arrhythmia focus or the exit of a reentry circuit in the border of a ventricular scar, but can be misleading in diseased ventricles. In structurally normal hearts, monomorphic VT is often referred to as idiopathic. In structural heart disease, sustained monomorphic VT is usually due to reentry involving a region of myocardial scar. Evidence of scar may be seen as areas of ventricular akinesis or dyskinesis on ventriculography, echocardiography, or cardiac magnetic resonance imaging (MRI) as areas of delayed gadolinum (Gd) washout.[1–3] In fewer than 10% of the patients, VT is due to bundle branch reentry through a diseased His-Purkinje system.[4]

Polymorphic VT indicates a varying ventricular activation sequence, and structural heart disease is not required. If prolonged, it usually degenerates to ventricular fibrillation (VF). Acute myocardial ischemia during an acute coronary syndrome is the most common cause, and following survival past an acute infarction, it does not predict a late risk of sudden death.[5] A number of genetically determined syndromes including long QT syndromes, Brugada syndrome, and short QT syndromes as well as catecholaminergic polymorphic VT cause polymorphic VT.[6]

Ventricular arrhythmias in the absence of structural heart disease

Idiopathic ventricular arrhythmias (premature ventricular beats, nonsustained VT, or commonly sustained monomorphic VT) typically present with palpitations and less commonly more severe symptoms including syncope.[7] A focal origin from the right ventricular (RV) or left ventricular (LV) outflow regions, which usually produces a left bundle branch block–like QRS morphology and inferior axis, is most common, followed by sites along an atrioventricular (AV) valve annulus or papillary muscle.[8–11] Less commonly, reentry involving fascicles of the LV Purkinje system causes a right bundle branch block–like idiopathic VT.[12] With an otherwise normal ECG, the absence of structural heart disease on cardiac imaging, and no evidence of a genetic arrhythmogenic syndrome, sudden death is rare and many patients require only reassurance.[2,7] For patients who require therapy, beta-blockers, verapamil or diltiazem, and other antiarrhythmic drugs can be helpful, but catheter ablation is often a preferred option to long-term drug therapy (see below).

Sudden death, ventricular dysfunction, and "idiopathic" arrhythmias

Rare patients with apparently idiopathic VT have suffered cardiac arrest.[2] Markers of increased risk have been suggested to be unusually rapid VT, a short initial coupling interval, and polymorphic VT.[13,14] Rare patients have recurrent VF or polymorphic VT initiated by premature

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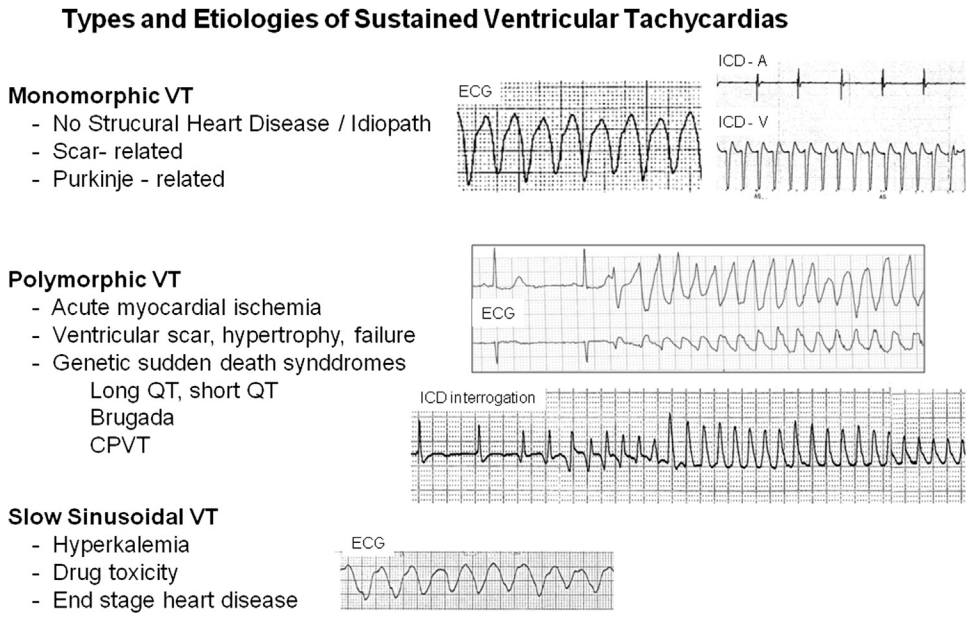

Figure 1 Electrocardiographic types of VT with examples of a surface ECG lead and ICD interrogation are shown with the common etiologic considerations. ECG = electrocardiographic/electrocardiogram; ICD = implantable cardioverter-defibrillator; VT = ventricular tachycardia

ventricular contractions (PVCs) from the Purkinje system or RV outflow tract that can be treated with ablation with a low risk of recurrence (Figure 2).[15]

An idiopathic arrhythmia is occasionally an early manifestation of underlying cardiomyopathy. For the common left bundle branch block–like arrhythmias, an RV origin is suspected. Arrhythmogenic right ventricular cardiomyopathy (ARVC) and cardiac sarcoidosis involving the RV are considerations, particularly if there are inverted T waves in leads V_1 to V_3 or AV conduction abnormalities are present.[2,16,17] Small areas of slow conduction and scar in the RV can escape detection in MRI but can be apparent as abnormal electrograms during epicardial mapping.[18] Rarely, a patient with no detectable structural abnormality subsequently develops evidence of heart disease.

Frequent PVCs can produce ventricular dysfunction in a manner perhaps similar to tachycardia-induced cardiomyopathy.[19] In most cases, more than 20% of ambient beats are ectopic.[20] It is often not clear whether an underlying cardiomyopathic process is present or measurement of the LV ejection fraction is not accurate owing to the presence of arrhythmia. The suppression of the arrhythmia and reassessment of ventricular function is required to sort out the possibilities. These observations support continued follow-up of patients with apparently idiopathic arrhythmias.

Catheter ablation in structurally normal hearts: Efficacy, risks, and challenges

Although catheter ablation is often effective for these arrhythmias, its overall efficacy is not well characterized

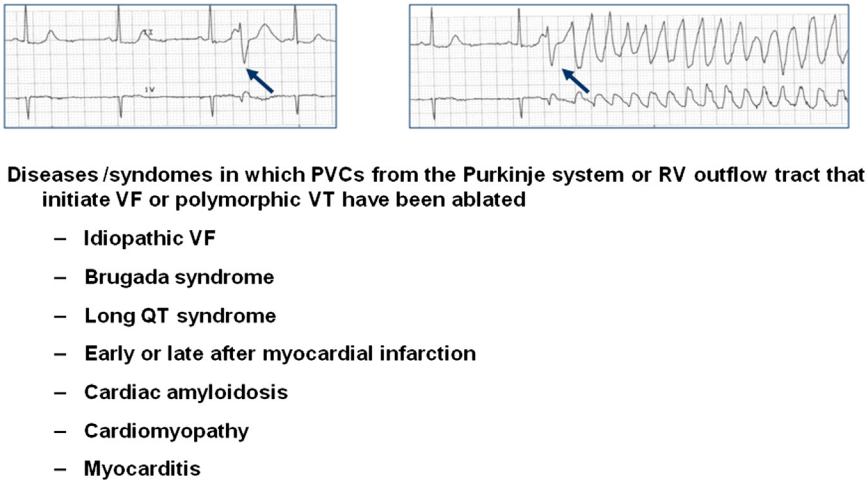

Figure 2 Recordings from a patient with idiopathic VF showing a premature ventricular beat in sinus rhythm (top left panel) and a premature ventricular beat that initiates polymorphic VT (top right panel). Ablation targeting this PVC focus (not shown) abolished recurrent VF episodes. PVC = premature ventricular contraction; RV = right ventricular; VF = ventricular fibrillation; VT = ventricular tachycardia.

because reports are largely limited to single centers, affected by referral bias, and exclude some patients who do not have inducible arrhythmia. Despite these issues, success rates are likely more than 80%.[7] There are, however, many challenges.

Ablation failure is perhaps most commonly due to inability to induce arrhythmia for adequate mapping. Our approach is to place ECG leads on the patient on arrival in the electrophysiology laboratory and immediately record any spontaneous arrhythmias so that they can potentially be used to guide pace mapping if the arrhythmia becomes quiescent. Although pace mapping can be used to guide ablation, it is less accurate than activation mapping.[7] In the periaortic region, pace mapping can be misleading and is often not helpful.[21] The provocation of idiopathic arrhythmias often requires intravenous administration of isoproterenol or epinephrine, sometimes combined with programmed stimulation and/or burst pacing from the ventricles or the atrium. Arm exercise and boluses of calcium, aminophylline, or phenylephrine have also been used, but in our experience, they are not usually helpful if boluses of intravenous medication have failed.

When arrhythmia is present but ablation fails, incomplete mapping is often the cause.[11] Outflow tract anatomy is complex. Focal arrhythmias can originate either from sleeves of muscle that extend above the pulmonary artery or aortic annulus or from epicardial sites. The electrogram at the target site can be of low amplitude and easily missed. Intracardiac ultrasound to define anatomy can be extremely helpful. For left bundle branch block inferior axis VT/PVCs, a systematic exploration of the RV outflow tract, pulmonary artery, and great cardiac vein/anterior interventricular vein region via the coronary sinus followed by the aortic root and LV outflow region is required. Some locations beneath the left coronary artery and deep within the interventricular septum are not accessible.[22,23] Surgical ablation is occasionally a consideration when severe symptoms or depressed ventricular function are present.[24] Idiopathic arrhythmias originating from the epicardium are most often found by mapping in a coronary vein.[25] Limited radiofrequency (RF) power delivery owing to low surrounding blood flow and proximity to adjacent coronary arteries can prevent successful ablation.[7] For ventricular ectopy originating from the papillary muscles, achieving adequate catheter stability is often challenging.[26]

Ablation complications of idiopathic arrhythmias are infrequent and vary with the arrhythmia location. In the free wall of the RV, perforation with tamponade is a concern.[27] Avoiding steam pops during RF application is important. For those that originate adjacent to the membranous septum, there is a potential risk of damage to the AV conduction system and AV block. In the aortic cusps, there is a risk of coronary injury if the catheter moves into a coronary ostium. Damage to the aortic valve can occur with catheter manipulation in the aortic root or potentially with delivery of RF energy on the aortic valve. In the epicardium or cardiac veins, coronary injury is the major concern.[7,28] Anticoagulation is warranted during aortic and LV procedures, and thromboembolism appears rare.

Ventricular arrhythmias in structural heart disease

VT leading to VF is an important cause of sudden death in almost all forms of heart disease, contributing to more than 350,000 out-of-hospital sudden deaths that occur annually in the United States.[29] Various mechanisms are operative. Implantable cardioverter-defibrillators (ICDs) remain the best protection against sudden death from ventricular arrhythmias in high-risk individuals, but most sudden deaths occur in individuals who do not have recognized high-risk profiles. Antiarrhythmic drugs and catheter ablation are largely reserved for controlling recurrent symptomatic arrhythmias in patients with ICDs.

ICDs

ICDs effectively terminate VT or VF. Patients who have been resuscitated from VT or VF that is not due to a cause that is reliably addressed with other therapy are at a particularly high risk of recurrence and usually warrant implantation of an ICD (referred to as secondary prevention of sudden death). Individuals who have not had sustained VT or VF, but whose heart disease places them at an increased risk may warrant an ICD for the primary prevention of sudden death (Table 1).[30,31] Remote monitoring provides the capability of interrogating the device at home and transmitting arrhythmia event and device data that facilitates early recognition of problems and can help reduce hospitalizations.[32,33] There are several challenges.

Table 1 Expected survival and reduction in mortality attributed to the ICD in primary prevention trials[30]

ICD indication: All assume expected 1-y survival with reasonable functional capacity	Trial	Survival with ICD (%)	Duration (y)	Absolute reduction in mortality with ICD (%)
LVEF <0.35 with NYHA class II or III heart failure	SCD-HeFT	71	5	7
Prior MI, LVEF ≤ 0.30	MADIT II	88	2	6
Prior MI, LVEF ≤ 0.40 + inducible VT	MUSTT	76	5	24
Diseases associated with a sudden death risk: ARVC, cardiac sarcoidosis, HCM, and other genetic syndromes with markers of risk	Observational studies	NA	NA	Unknown

ARVC = arrhythmogenic right ventricular cardiomyopathy; HCM = hypertrophic cardiomyopathy; ICD = implantable cardioverter-defibrillator; LVEF = left ventricular ejection fraction; MADIT II = Multicenter Automatic Defibrillator Implantation Trial II; MI = myocardial infarction; MUSTT = Multicenter Unsustained Tachycardia Trial; NA = not applicable; NYHA = New York Heart Association; SCD-HeFT = Sudden Cardiac Death in Heart Failure Trial.

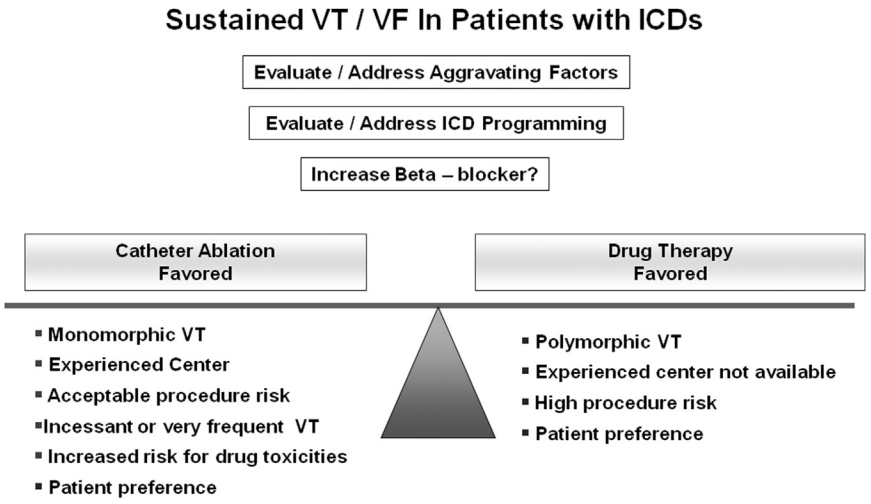

Figure 3 Illustration of an approach to the patient with an ICD who has a VT recurrence. ICD = implantable cardioverter-defibrillator; VF = ventricular fibrillation; VT = ventricular tachycardia.

The selection of patients for primary prevention ICDs remains imperfect.[30] Most are implanted on the basis of a low LV ejection fraction.[30,34] Although the majority of patients will not have spontaneous arrhythmias requiring therapy and the absolute survival benefit in trials was modest (Table 1), a survival benefit is also supported by analysis in populations outside trials.[31,34–36] ICDs are not warranted for patients who have a limited life expectancy and poor functional capacity owing to comorbid conditions. Functional limitations of heart failure may be improved; however, for those who have QRS prolongation owing to left bundle branch block, two-thirds will improve with biventricular pacing that can be implemented with the ICD.[37] ICDs are important options for genetic diseases that cause sudden death including hypertrophic cardiomyopathy, ARVC, Brugada syndrome, and some individuals with long QT syndrome.[38] Progress is being made in the selection of high-risk individuals with various diseases.

ICD lead malfunctions remain a concern that subjects the patient to the risks of inappropriate therapy, failure of needed therapy, and risk of surgical revision of the ICD system, with either lead extraction or addition of a new lead.[39] Leadless defibrillators should reduce risks related to leads, but have other limitations that require ongoing study.[40]

Some observations suggest that the initial landmark studies actually underestimate the benefit of providing effective arrhythmia termination because ICDs do have potential adverse effects that offset some of the benefit.[39–42] Initially unappreciated was the possibility that the implanted device could have adverse effects that partially offset the mortality benefit, as was dramatically observed in the Dual Chamber and VVI Implantable Defibrillator trial,[41] in which programming that increased RV pacing increased mortality, likely through aggravation of ventricular dysfunction. Programming to avoid RV pacing became standard practice, and device algorithms were developed to attempt to minimize ventricular pacing. Backup pacing for bradycardia also has the potential to cause long-short sequences that initiate ventricular arrhythmias in some patients.[42] Unnecessary antitachycardia pacing therapy in response to supraventricular arrhythmias or electrical noise sometimes induces ventricular arrhythmias.[43] Proarrhythmia may contribute to the consistent observation in randomized trials: that the number of patients with arrhythmia termination from an ICD substantially exceeds the mortality benefit.[44]

ICD arrhythmia detection algorithms are also important. The Multicenter Automatic Defibrillator Implantation Trial—Reduce Inappropriate Therapy compared different VT detection criteria in patients who received a primary prevention ICD.[43] The conventional programming strategy that treated VT that was faster than 170 beats/min lasting for 2.5 seconds resulted in more ICD therapies (shocks and antitachycardia pacing) compared to strategies to treat VT only after 60 seconds, or only if VT was faster than 200 beats/min. Surprisingly, the mortality was greater with conventional programming: 10% at 2 years compared to 7% and 5% in the delayed detection and high rate groups, respectively. The reasons for the increase in mortality are not clear, but arrhythmias detected and treated by the ICD have been associated with reduced survival and increased heart failure hospitalizations in other studies.[45–47] Arrhythmias, whether spontaneous or induced by the ICD, may be a marker for progression of underlying heart disease. It is also possible that ICD shocks cause direct myocardial damage and sympathetic activation.[47,48] Most VTs, however, can be terminated by antitachycardia pacing, which has been associated with lower mortality compared to shocks.[47] In any case, because of these considerations and the potential negative effect of ICD shocks on quality of life, the prevention of spontaneous episodes of VT with drugs or ablation is important (Figure 3).[49]

Antiarrhythmic drug therapy

Antiarrhythmic drug efficacy for preventing arrhythmias has been disappointing, but they have a role in reducing episodes

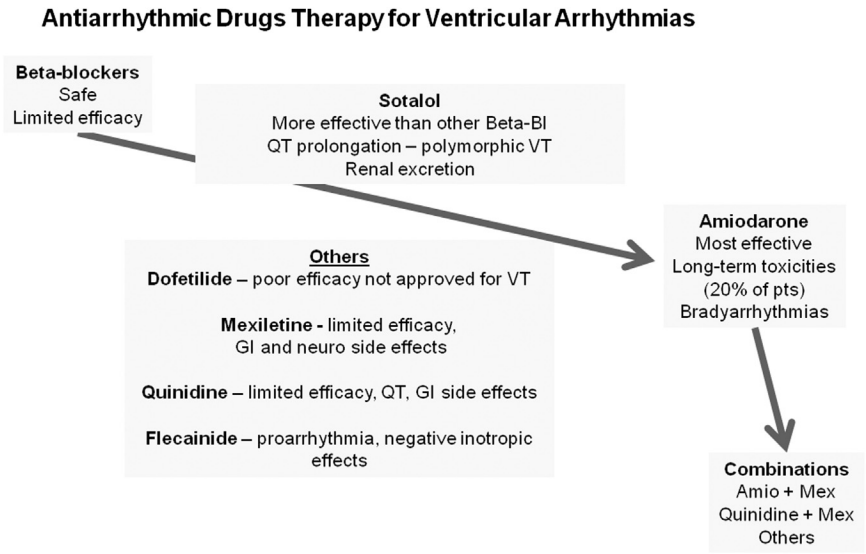

Figure 4 Illustration of an approach of a sequence of considerations for selecting antiarrhythmic drugs to treat ventricular arrhythmias. For most patients with advanced heart disease, amiodarone will be selected. GI = gastrointestinal; VT = ventricular tachycardia.

(Figure 4). Arrhythmias are often aggravated by increased sympathetic tone.[50] Beta-blockers are relatively safe and reduce sudden death in patients with heart failure or LV dysfunction after myocardial infarction. Unfortunately, their efficacy for preventing recurrent VT is often poor. The combined beta-blocker, rapidly activating component of the delayed rectifier potassium current (I_{Kr}) blocker sotalol, is somewhat more effective.[51] Amiodarone is the most effective drug, but more than 20% of the patients have VT recurrences.[51] Adverse effects limit therapy in more than 20% of the patients, including thyroid, neurologic, and, less commonly, lung or liver toxicity. Proarrhythmic effects and ICD interactions, most commonly slowing a VT below the ICD detection rate, are important concerns with drug therapy. Development of new pharmacologic approaches to antiarrhythmic therapy is a major challenge.

Catheter ablation

Catheter ablation has an important role in reducing arrhythmias in patients with ICDs and can be lifesaving for patients with incessant or frequent VT.[7,52] It has generally been reserved for patients with monomorphic VT, but it can also be effective for recurrent polymorphic VT and VF when initiating PVCs can be targeted (Figure 2).

More than 90% of the sustained monomorphic VTs in patients with heart disease are due to reentry involving an area of ventricular scar. The remaining VTs are due to reentry or automaticity involving the Purkinje system and are often more easily targeted for ablation.[4] The scar-related arrhythmia substrate is stable, so approximately half of the patients who present with monomorphic VT will have a recurrence within 2 years.[53] The efficacy of catheter ablation for scar-related reentry depends on the location of the reentry circuit and the ability to identify the circuit. VT due to prior myocardial infarction has been best studied. The majority of these VTs can be approached from the endocardium. Most studies have enrolled patients with recurrent VT that is failing antiarrhythmic drug therapy and who have severely depressed ventricular function. In multicenter studies, ablation reduces or abolishes VT in approximately 70% of the patients; however, approximately 26%–50% will experience at least 1 spontaneous episode of VT detected by the ICD during follow-up.[7,53–55] The procedure morality is 3%, with most deaths owing to uncontrollable VT when the procedure fails.[55] Total mortality in this population is as high as 18% at 1 year, likely reflecting the fact that recurrent VT is often a marker of severe disease.[55] The optimal approach to ablation is still evolving, and there are many challenges and questions.

VTs are characterized by their QRS morphology, which is determined largely by the location of the reentry circuit exit in the border of the scar, and rate.[7] Multiple VTs are often inducible with programmed stimulation, suggesting the presence of multiple reentry circuits and/or reentry circuit exits. VTs that have been observed to occur spontaneously are designated "clinical VTs." The best end point for ablation has not been defined, although persistent inducibility of a clinical VT has been associated with recurrent VT and some centers attempt to abolish all inducible VTs.[7] When mapping can be performed during VT, a critical channel can often be identified with a combination of limited activation and entrainment mapping where limited ablation interrupts the VT circuit. More commonly, hemodynamic instability or the presence of multiple inducible VTs limits mapping during VT. Hemodynamic support during VT with a percutaneous assist device or cardiopulmonary bypass can allow more detailed mapping during VT and warrants further evaluation.[52,56] Another approach is to deploy a multielectrode catheter for sampling during short runs of VT. The "noncontact" system that mathematically reconstructs electrograms is often able to indicate exit regions, but cannot usually detect channels.

The most common approach to guide ablation for multiple and unstable VTs is *substrate mapping*, which identifies

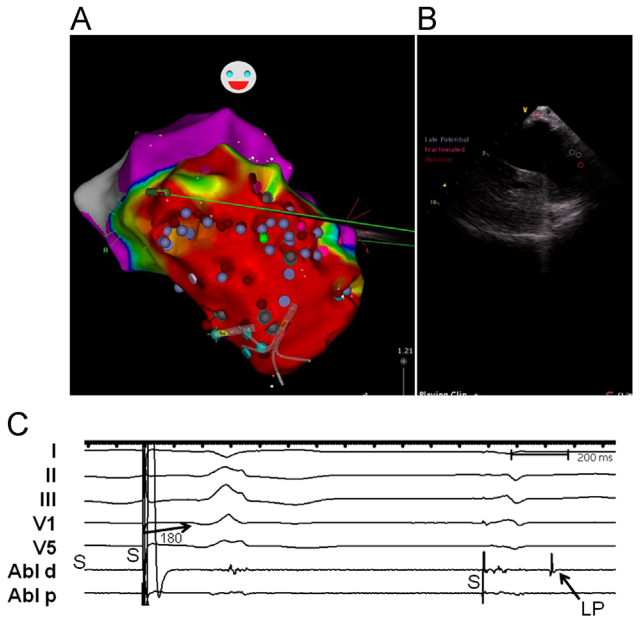

Figure 5 Recordings from a patient with prior anteroseptal infarct and recurrent VT, illustrating findings during substrate mapping. **A:** An LV voltage map (left anterior projection) with purple color indicating a bipolar voltage > 1.5 mV, and a large low-voltage scar (red, yellow, green, blue area). **B:** The intracardiac ultrasound imaging corresponding to the planar slide of the ultrasound beam seen in panel A. **C:** The last beat of pace mapping from the ablation catheter at a site with a long S-QRS interval of 180 ms in the low-voltage area. After termination of LV pace mapping, an LP is seen with the RV paced beat at the right side of the panel (arrow). Abl = ablation; d = distal; LP = late potential; LV = left ventricular; p = proximal; RV = right ventricular; VT = ventricular tachycardia.

the VT substrate during stable sinus or paced rhythm (Figure 5).[7] Substrate mapping is extremely useful and routinely used for most scar-related VTs; even when VT is stable it is often combined with activation and entrainment mapping. Ventricular anatomy is reconstructed in an electroanatomic mapping system with point-by-point mapping, intracardiac ultrasound, or registration of a prior imaging study. The bipolar electrogram amplitude from contact mapping is displayed on the anatomy in a voltage map. Regions with a bipolar electrogram amplitude < 1.5 mV indicate regions where myocytes have been replaced, or partially replaced by fibrous tissue. MRI studies have shown that this threshold is conservative, and there is often fibrosis deep to the endocardium that extends beyond the edge of the 1.5 mV endocardial border.[3,57] Intramural and epicardial scar is not detectable based on this bipolar electrogram amplitude, but exploiting the greater "field of view" of unfiltered or minimally filtered unipolar electrograms, epicardial and intramural scar can often be identified from endocardial unipolar electrogram voltage maps as regions of relatively lower voltage despite bipolar electrograms exceeding 1.5 mV. Markers of potential channels in and around the low-voltage scar area include multicomponent, fractionated electrograms, and split and late potentials, which indicate separation of myocyte bundles by fibrosis that is a cause of slow conduction.[7,58,59] Pacing can be performed from the mapping catheter (pace mapping) to identify sites where pacing fails to capture, indicative of fibrosis without surviving myocytes, termed electrically unexcitable scar.[60,61] Sites where pacing replicates the QRS morphology of VT are often near the VT exit, and long stimulus to QRS delays (Figure 5) indicate slow conduction and potentials channels. The best ablation strategy is not clear. Approaches targeting electrograms, interesting pace-mapping sites, and completely covering the low-voltage region with RF applications have been reported, but not directly compared in randomized studies.[7,59–62]

The location of the arrhythmia substrate and success of ablation varies with the underlying disease.[63] The procedure is most often successful in patients with prior myocardial infarction, ARVC, and repaired tetralogy of Fallot, in whom the potential reentry channels are now well defined.[64] Ablation is more likely to be difficult in nonischemic cardiomyopathies when the circuits are intramural or epicardial in locations protected by coronary arteries.[63,65,66]

Subepicardial arrhythmia substrate can often be approached by percutaneous pericardial access, which is often needed in nonischemic cardiomyopathies, particularly ARVC.[67,68] Major complications, most commonly bleeding, occur in approximately 5% of the patients.[69,70] Precautions to avoid injury to coronary arteries and the left phrenic nerve are important.[28]

Ablation failure often indicates inability to achieve an adequate, durable effect on the arrhythmia substrate.[59] Transcoronary ethanol ablation targeting the arrhythmogenic area is used in approximately 1.5% of the patients with VT that has failed other means of ablation at our center, but is often limited by failure to identify a coronary target and has the potential for damage to large areas of myocardium.[71] Surgical ablation remains an option as well.[24]

A look ahead

The integral role of devices in the management of high-risk patients, particularly those with heart failure, seems likely to increase with advances in pacing, programming, and monitoring capabilities. Technologic complexities, implementation, and reducing infection remain important challenges. Imaging to better characterize the arrhythmia substrate continues to improve and will hopefully facilitate the recognition of high-risk substrate, thereby identifying patients who would benefit from an ICD, as well as guiding ablation and perhaps directing biological therapies to the arrhythmia substrate.[1,57,72]

We continue to see patients with posttraumatic stress disorder from ICD shocks,[49] supporting a role for an earlier use of ablation to reduce recurrences and further studies are needed to clarify best strategies and the effects on mortality and costs.[53,73,74] A needle injection catheter has shown promise for reaching intramural regions for ablation.[75] Pharmacologic and device therapies that modulate neural systems will provide new therapeutic options.[50] Ultimately, combinations of devices, ablation, pharmacologic, and biological therapies will further reduce arrhythmias and sudden

death risk while continuing to improve ventricular function and slow adverse remodeling. These latter aspects are critical, as, even with arrhythmia control, the mortality remains substantial in patients with structural heart disease and arrhythmias. Although progress has been substantial, many challenges remain.

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References

1. Andreu D, Berruezo A, Ortiz-Perez JT, et al. Integration of 3D electroanatomic maps and magnetic resonance scar characterization into the navigation system to guide ventricular tachycardia ablation. Circ Arrhythm Electrophysiol 2011;4:674–683.
2. Aquaro GD, Pingitore A, Strata E, et al. Cardiac magnetic resonance predicts outcome in patients with premature ventricular complexes of left bundle branch block morphology. J Am Coll Cardiol 2011;56:1235–1243.
3. Wijnmaalen AP, van der Geest RJ, van Huls van Taxis CF, et al. Head-to-head comparison of contrast-enhanced magnetic resonance imaging and electroanatomical voltage mapping to assess post-infarct scar characteristics in patients with ventricular tachycardias. Eur Heart J 2010;32:104–114.
4. Lopera G, Stevenson WG, Soejima K, et al. Identification and ablation of three types of ventricular tachycardia involving the His-Purkinje system in patients with heart disease. J Cardiovasc Electrophysiol 2004;15:52–58.
5. Mehta RH, Starr AZ, Lopes RD, et al. Incidence of and outcomes associated with ventricular tachycardia or fibrillation in patients undergoing primary percutaneous coronary intervention. JAMA 2009;301:1779–1789.
6. Sy RW, Gollob MH, Klein GJ, et al. Arrhythmia characterization and long-term outcomes in catecholaminergic polymorphic ventricular tachycardia. Heart Rhythm 2011;8:864–871.
7. Aliot EM, Stevenson WG, Almendral-Garrote JM, et al. EHRA/HRS expert consensus on catheter ablation of ventricular arrhythmias. Heart Rhythm 2009;6:886–933.
8. Yamada T, Doppalapudi H, McElderry HT, et al. Electrocardiographic and electrophysiological characteristics in idiopathic ventricular arrhythmias originating from the papillary muscles in the left ventricle: relevance for catheter ablation. Circ Arrhythm Electrophysiol 2010;3:324–331.
9. Yamada T, Doppalapudi H, McElderry HT, et al. Idiopathic ventricular arrhythmias originating from the papillary muscles in the left ventricle. J Cardiovasc Electrophysiol 2010;21:62–69.
10. Van Herendael H, Garcia F, Lin D, et al. Idiopathic right ventricular arrhythmias not arising from the outflow tract: prevalence, electrocardiographic characteristics, and outcome of catheter ablation. Heart Rhythm 2010;8:511–518.
11. Yokokawa M, Good E, Crawford T, et al. Reasons for failed ablation for idiopathic right ventricular outflow tract-like ventricular arrhythmias. Heart Rhythm 2013;10:1101–1108.
12. Nogami A, Naito S, Tada H, et al. Demonstration of diastolic and presystolic purkinje potentials as critical potentials in a macroreentry circuit of verapamil-sensitive idiopathic left ventricular tachycardia. J Am Coll Cardiol 2000;36:811–823.
13. Igarashi M, Tada H, Kurosaki K, et al. Electrocardiographic determinants of the polymorphic QRS morphology in idiopathic right ventricular outflow tract tachycardia. J Cardiovasc Electrophysiol 2012;23:521–526.
14. Shimizu W. Arrhythmias originating from the right ventricular outflow tract: how to distinguish "malignant" from "benign"? Heart Rhythm 2009;6:1507–1511.
15. Knecht S, Sacher F, Wright M, et al. Long-term follow-up of idiopathic ventricular fibrillation ablation: a multicenter study. J Am Coll Cardiol 2009;54:522–528.
16. Basso C, Corrado D, Bauce B, Thiene G. Arrhythmogenic right ventricular cardiomyopathy. Circ Arrhythm Electrophysiol 2012;5:1233–1246.
17. Hoffmayer KS, Machado ON, Marcus GM, et al. Electrocardiographic comparison of ventricular arrhythmias in patients with arrhythmogenic right ventricular cardiomyopathy and right ventricular outflow tract tachycardia. J Am Coll Cardiol 2011;58:831–838.
18. Marra MP, Leoni L, Bauce B, et al. Imaging study of ventricular scar in arrhythmogenic right ventricular cardiomyopathy. Circ Arrhythm Electrophysiol 2012;5:91–100.
19. Yokokawa M, Good E, Crawford T, et al. Recovery from left ventricular dysfunction after ablation of frequent premature ventricular complexes. Heart Rhythm 2013;10:172–175.
20. Niwano S, Wakisaka Y, Niwano H, et al. Prognostic significance of frequent premature ventricular contractions originating from the ventricular outflow tract in patients with normal left ventricular function. Heart 2009;95:1230–1237.
21. Yamada T, Murakami Y, Yoshida N, et al. Preferential conduction across the ventricular outflow septum in ventricular arrhythmias originating from the aortic sinus cusp. J Am Coll Cardiol 2007;50:884–891.
22. Yamada T, McElderry HT, Doppalapudi H, et al. Idiopathic ventricular arrhythmias originating from the left ventricular summit: anatomic concepts relevant to ablation. Circ Arrhythm Electrophysiol 2010;3:616–623.
23. Yokokawa M, Good E, Chugh A, et al. Intramural idiopathic ventricular arrhythmias originating in the intraventricular septum: mapping and ablation. Circ Arrhythm Electrophysiol 2012;5:258–263.
24. Anter E, Hutchinson MD, Deo R, et al. Surgical ablation of refractory ventricular tachycardia in patients with nonischemic cardiomyopathy. Circ Arrhythm Electrophysiol 2011;4:494–500.
25. Daniels DV, Lu YY, Morton JB, et al. Idiopathic epicardial left ventricular tachycardia originating remote from the sinus of valsalva. Circulation 2006;113:1659–1666.
26. Yamada T, Doppalapudi H, McElderry HT, et al. Electrocardiographic and electrophysiological characteristics in idiopathic ventricular arrhythmias originating from the papillary muscles in the left ventricle. Circ Arrhythm Electrophysiol 2011;3:324–331.
27. Tokuda M, Kojodjojo P, Epstein LM, et al. Outcomes of cardiac perforation complicating catheter ablation of ventricular arrhythmias. Circ Arrhythm Electrophysiol 2011;4:660–666.
28. Roberts-Thomson KC, Steven D, Seiler J, et al. Coronary artery injury due to catheter ablation in adults: presentations and outcomes. Circulation 2009;120:1465–1473.
29. Go AS, Mozaffarian D, Roger VL, et al. Heart disease and stroke statistics—2013 update: a report from the American Heart Association. Circulation 2013;127:e6–e245.
30. Hohnloser SH, Israel CW. Current evidence base for use of the implantable cardioverter-defibrillator. Circulation 2013;128:172–183.
31. Al-Khatib SM, Hellkamp A, Bardy GH, et al. Survival of patients receiving a primary prevention implantable cardioverter-defibrillator in clinical practice vs clinical trials. JAMA 2013;309:55–62.
32. Crossley GH, Boyle A, Vitense H, et al. The connect (clinical evaluation of remote notification to reduce time to clinical decision) trial: the value of wireless remote monitoring with automatic clinician alerts. J Am Coll Cardiol 2011;57:1181–1189.
33. Landolina M, Perego GB, Lunati M, et al. Remote monitoring reduces healthcare use and improves quality of care in heart failure patients with implantable defibrillators. Circulation 2012;125:2985–2992.
34. Epstein AE, DiMarco JP, Ellenbogen KA, et al. ACC/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities. Circulation 2008;117:e350–e408.
35. Parkash R, Sapp JL, Basta M, et al. Use of primary prevention implantable cardioverter-defibrillators in a population-based cohort is associated with a significant survival benefit. Circ Arrhythm Electrophysiol 2012;5:706–713.
36. Hulleman M, Berdowski J, de Groot JR, et al. Implantable cardioverter-defibrillators have reduced the incidence of resuscitation for out-of-hospital cardiac arrest caused by lethal arrhythmias. Circulation 2012;126:815–821.
37. Finegold JA, Raphael C, Levy WC, Winnett Z, Francis DP. Quantification of survival gain from cardiac resynchronization therapy: non-linear growth with time, and greater gain in low-risk patients, make raw trial data an underestimate of real-world behaviour. J Am Coll Cardiol 2013. (XX:XX–XX).
38. Olde Nordkamp LR, Wilde AA, Tijssen JG, et al. The ICD for primary prevention in patients with inherited cardiac diseases. Circ Arrhythm Electrophysiol 2013;6:91–100.
39. Maytin M, Jones SO, Epstein LM. Long-term mortality after transvenous lead extraction. Circ Arrhythm Electrophysiol 2012;5:252–257.
40. Bardy GH, Smith WM, Hood MA, et al. An entirely subcutaneous implantable cardioverter-defibrillator. N Engl J Med 2010;363:36–44.
41. Wilkoff BL. The Dual Chamber and VVI Implantable Defibrillator (DAVID) trial: rationale, design, results, clinical implications and lessons for future trials. Card Electrophysiol Rev 2003;7:468–472.
42. Sweeney MO, Ruetz LL, Belk P, et al. Bradycardia pacing-induced short-long-short sequences at the onset of ventricular tachyarrhythmias: a possible mechanism of proarrhythmia? J Am Coll Cardiol 2007;50:614–622.

43. Moss AJ, Schuger C, Beck CA, et al. Reduction in inappropriate therapy and mortality through ICD programming. N Engl J Med 2012;367:2275–2283.
44. Ellenbogen KA, Levine JH, Berger RD, et al. Are implantable cardioverter defibrillator shocks a surrogate for sudden cardiac death in patients with nonischemic cardiomyopathy? Circulation 2006;113:776–782.
45. Powell BD, Saxon LA, Boehmer JP, et al. Survival after shock therapy in ICD and CRT-D recipients according to rhythm shocked: altitude survival by rhythm study. J Am Coll Cardiol 2013.
46. Saxon LA, Hayes DL, Gilliam FR, et al. Long-term outcome after ICD and CRT implantation and influence of remote device follow-up: the altitude survival study. Circulation 2010;122:2359–2367.
47. Sweeney MO, Sherfesee L, DeGroot PJ, Wathen MS, Wilkoff BL. Differences in effects of electrical therapy type for ventricular arrhythmias on mortality in implantable cardioverter-defibrillator patients. Heart Rhythm 2010;7:353–360.
48. Toh N, Nishii N, Nakamura K, et al. Cardiac dysfunction and prolonged hemodynamic deterioration after implantable cardioverter-defibrillator shock in patients with systolic heart failure. Circ Arrhythm Electrophysiol 2012;5:898–905.
49. Sears SF, Hauf JD, Kirian K, Hazelton G, Conti JB. Posttraumatic stress and the implantable cardioverter-defibrillator patient: what the electrophysiologist needs to know. Circ Arrhythm Electrophysiol 2011;4:242–250.
50. Bourke T, Vaseghi M, Michowitz Y, et al. Neuraxial modulation for refractory ventricular arrhythmias: value of thoracic epidural anesthesia and surgical left cardiac sympathetic denervation. Circulation 2010;121:2255–2262.
51. Connolly SJ, Dorian P, Roberts RS, et al. Comparison of beta-blockers, amiodarone plus beta-blockers, or sotalol for prevention of shocks from implantable cardioverter defibrillators. The optic study: A randomized trial. JAMA 2006;295:165–171.
52. Carbucicchio C, Santamaria M, Trevisi N, et al. Catheter ablation for the treatment of electrical storm in patients with implantable cardioverter-defibrillators: short- and long-term outcomes in a prospective single-center study. Circulation 2008;117:462–469.
53. Kuck KH, Schaumann A, Eckardt L, et al. Catheter ablation of stable ventricular tachycardia before defibrillator implantation in patients with coronary heart disease (VTACH): a multicentre randomised controlled trial. Lancet 2010;375:31–40.
54. Dinov B, Schonbauer R, Wojdyla-Hordynska A, et al. Long-term efficacy of single procedure remote magnetic catheter navigation for ablation of ischemic ventricular tachycardia: a retrospective study. J Cardiovasc Electrophysiol 2012;23:499–505.
55. Stevenson WG, Wilber DJ, Natale A, et al. Irrigated radiofrequency catheter ablation guided by electroanatomic mapping for recurrent ventricular tachycardia after myocardial infarction. Circulation 2008;118:2773–2782.
56. Miller MA, Dukkipati SR, Chinitz JS, et al. Percutaneous hemodynamic support with impella 2.5 during scar-related ventricular tachycardia ablation (PERMIT 1). Circ Arrhythm Electrophysiol 2013;6:151–159.
57. Sasaki T, Miller CF, Hansford R, et al. Myocardial structural associations with local electrograms: a study of postinfarct ventricular tachycardia pathophysiology and magnetic resonance-based noninvasive mapping. Circ Arrhythm Electrophysiol 2012;5:1081–1090.
58. (de) Bakker JM, Wittkampf FH. The pathophysiologic basis of fractionated and complex electrograms and the impact of recording techniques on their detection and interpretation. Circ Arrhythm Electrophysiol 2010;3:204–213.
59. Jais P, Maury P, Khairy P, et al. Elimination of local abnormal ventricular activities: a new end point for substrate modification in patients with scar-related ventricular tachycardia. Circulation 2012;125:2184–2196.
60. Soejima K, Stevenson WG, Maisel WH, Sapp JL, Epstein LM. Electrically unexcitable scar mapping based on pacing threshold for identification of the reentry circuit isthmus: feasibility for guiding ventricular tachycardia ablation. Circulation 2002;106:1678–1683.
61. Tung R, Mathuria N, Michowitz Y, et al. Functional pace-mapping responses for identification of targets for catheter ablation of scar-mediated ventricular tachycardia. Circ Arrhythm Electrophysiol 2012;5:264–272.
62. Di Biase L, Santangeli P, Burkhardt DJ, et al. Endo-epicardial homogenization of the scar versus limited substrate ablation for the treatment of electrical storms in patients with ischemic cardiomyopathy. J Am Coll Cardiol 2012;60:132–141.
63. Tokuda M, Tedrow UB, Kojodjojo P, et al. Catheter ablation of ventricular tachycardia in nonischemic heart disease. Circ Arrhythm Electrophysiol 2012;5:992–1000.
64. Zeppenfeld K, Schalij MJ, Bartelings MM, et al. Catheter ablation of ventricular tachycardia after repair of congenital heart disease: electroanatomic identification of the critical right ventricular isthmus. Circulation 2007;116:2241–2252.
65. Desjardins B, Yokokawa M, Good E, et al. Characteristics of intramural scar in patients with non-ischemic cardiomyopathy and relation to intramural ventricular arrhythmias. Circ Arrhythm Electrophysiol 2013.
66. Piers SR, Leong DP, van Huls van Taxis CF, et al. Outcome of ventricular tachycardia ablation in patients with nonischemic cardiomyopathy: the impact of noninducibility. Circ Arrhythm Electrophysiol 2013.
67. Philips B, Madhavan S, James C, et al. Outcomes of catheter ablation of ventricular tachycardia in arrhythmogenic right ventricular dysplasia/cardiomyopathy. Circ Arrhythm Electrophysiol 2012;5:499–505.
68. Berruezo A, Fernandez-Armenta J, Mont L, et al. Combined endocardial and epicardial catheter ablation in arrhythmogenic right ventricular dysplasia incorporating scar dechanneling technique. Circ Arrhythm Electrophysiol 2012;5:111–121.
69. Della Bella P, Brugada J, Zeppenfeld K, et al. Epicardial ablation for ventricular tachycardia: a European multicenter study. Circ Arrhythm Electrophysiol 2011;4:653–659.
70. Sacher F, Roberts-Thomson K, Maury P, et al. Epicardial ventricular tachycardia ablation a multicenter safety study. J Am Coll Cardiol 2010;55:2366–2372.
71. Tokuda M, Sobieszczyk P, Eisenhauer AC, et al. Transcoronary ethanol ablation for recurrent ventricular tachycardia after failed catheter ablation: an update. Circ Arrhythm Electrophysiol 2011;4:889–896.
72. Estner HL, Zviman MM, Herzka D, et al. The critical isthmus sites of ischemic ventricular tachycardia are in zones of tissue heterogeneity, visualized by magnetic resonance imaging. Heart Rhythm 2011;8:1942–1949.
73. Pauriah M, Cismaru G, Magnin-Poull I, et al. A stepwise approach to the management of postinfarct ventricular tachycardia using catheter ablation as the first-line treatment: a single-center experience. Circ Arrhythm Electrophysiol 2013;6:351–356.
74. Reddy VY, Reynolds MR, Neuzil P, et al. Prophylactic catheter ablation for the prevention of defibrillator therapy. N Engl J Med 2007;357:2657–2665.
75. Sapp J, Beeckler C, Pike R, et al. Initial human feasibility of infusion needle catheter ablation for refractory ventricular tachycardia. Circulation 2013.