ECG Clues for Diagnosing Ventricular Tachycardia Mechanism

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ECG Clues to VT Mechanism. Three mechanisms underlie the initiation and maintenance of ventricular tachycardia: automaticity, triggered activity, and reentry. As straightforward as these mechanisms are, assessing which mechanism is operative in a particular patient's ventricular tachycardia can be difficult. The optimal treatment strategy for ventricular tachycardia in a given patient can be influenced by the mechanism underlying the ventricular tachycardia. Appropriately counseling patients, choosing the optimal pharmacologic agent that maximizes efficacy while minimizing undesirable side effects, risks, and toxicities, as well as recommending and timing ablative therapy all hinge on identifying the probable mechanism of ventricular tachycardia. Much has been published regarding invasive electrophysiologic maneuvers that allow for correct diagnosis of ventricular tachycardia mechanism. The aim of this clinical review is to provide insight into VT mechanisms based on ECG clues of spontaneous arrhythmia events and the response to pharmacologic manipulation prior to invasive electrophysiologic evaluation. (*J Cardiovasc Electrophysiol*, *Vol. 19, pp. 224-229, February 2008.*)

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Introduction

In contrast to the wealth of sites of origin of VT and the variability in substrate within which VT can arise, there remain only three identified mechanisms for VT: abnormal automaticity, triggered activity, and reentry. In spite of the limited options for mechanism, correct identification of the mechanism can be very difficult, yet it remains important in order to optimally treat VT. Most focal VTs, due to a triggered or automatic mechanism, are frequently amenable to beta blockade therapy and, in turn, focal ablative therapy. The 12-lead ECG provides a powerful tool for localizing the focal origin and the target for ablative therapy.¹⁻⁴ In contrast, reentrant VTs usually require membrane active antiarrhythmic agents that slow conduction or prolong refractoriness to prevent reentry. The 12-lead ECG of the VT may only identify an exit for a sizable macroreentrant circuit. The ablation strategy is frequently aimed at interrupting the width of the reentrant circuit by creating linear lesions of significant length. Clearly, the anticipation of the appropriate mechanism based on ECG clues and the response to pharmacologic manipulation should help set the course of the invasive electrophysiologic procedure.

Definitions and Clinical Examples

Normal automaticity refers to the mechanism by which the normal hierarchy of pacemaker cells (i.e., sinus node, AV node, His-purkinje system, and ventricle) maintains a reliable source of impulse formation. In this context, escape rhythms in the ventricle typically manifest at rates less than 50 bpm. In contrast, *abnormal automaticity* as a mechanism for ventricular tachycardia refers to the circumstance where a region of ventricular cells generates impulse formation at an accelerated rate compared with normal, due to an altered threshold for inward ventricular myocyte sodium influx. Accelerated idioventricular rhythms in the setting of acute ischemia, myocarditis, or cocaine intoxication are thought to be manifestations of abnormal automaticity.^{5,6}

Triggered activity refers to action potential formation resulting from oscillations in membrane potential that are dependent on the preceding action potential. Triggered activity can occur in the form of early or delayed afterdepolarizations. Early afterdepolarizations (EADs) occur during phase II or III of the action potential, are more manifest at slower rates, and have been shown to be mechanistically responsible for many forms of drug and electrolyte-induced Torsades de Pointes, and some forms of polymorphic VT due to congenital long QT syndrome. Delayed afterdepolarizations (DADs) occur during phase IV of the action potential, are more dependent on faster heart rates, and have been shown to be mechanistically responsible for many forms of outflow tract tachycardia and VT associated with digitalis toxicity.⁷⁻⁹

Reentrant ventricular tachycardia requires a specific electrophysiologic substrate or milieu: (1) unidirectional conduction, (2) conduction block, either fixed or functional, and (3) a region of "slow conduction" in which the cycle length of the tachycardia is longer than the longest refractory period in the circuit. Reentrant ventricular tachycardias are often seen

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in structurally abnormal myocardium characterized by scarring due to ischemic or nonischemic insults. The extensive scarring provides the abnormal anatomic and functional features to sustain the reentrant circuit. Critically timed impulses interact with the zones of slowed or absent conduction, setting up a loop of conduction around the fixed or functional conduction barriers.

For a given ventricular tachycardia, differentiating between these three mechanisms can be challenging. Invasive electrophysiologic maneuvers including reproducibility of initiation and termination in response to programmed stimulation, response to overdrive pacing (suppression, acceleration), and resetting responses to premature extrastimuli can usually provide enough evidence to reliably differentiate automatic, triggered, and reentrant rhythms. Noninvasive differentiation is much more difficult. However, there are several ECG and other clues that can help in this regard. Unfortunately, the currently available clues often serve either to exclude one of the potential three mechanisms or to strongly bias toward a particular mechanism without definitive proof. The limitation on the use of noninvasive tools to assess mechanism coupled with the importance of understanding mechanism, point to the importance of further research to develop ECG criteria and other noninvasive tools capable of differentiating among the three mechanisms.

Clues from the Sinus Rhythm ECG

Some of the most important clues to determining the mechanism of VT can be found with careful evaluation of the baseline sinus rhythm ECG. Patients with normal baseline ECGs and VT often have structurally normal hearts. Although VT due to any of the three mechanisms can occur in patients with structurally normal hearts, a normal baseline ECG coupled with specific and well-described morphologic patterns of VT can provide clues to the mechanism of a patient's VT. For instance, outflow tract tachycardias occur frequently in patients with structurally normal hearts and have been shown to be due to triggered activity (see below).^{7,9} In addition, fascicular VT is usually, but not always, due to a reentrant circuit involving the left posterior fascicle.¹⁰ An abnormal ECG suggestive of structural heart disease can, depending on the specific abnormality, lend evidence for reentrant VT. Q waves consistent with prior myocardial infarction (with or without ST/T-wave changes consistent with aneurysm) suggest the substrate for reentry within healed infarction scar, especially if the morphology of the VT is consistent with an exit from the region of the infarct. Interfascicular VT can also be observed in patients with prior myocardial infarction.¹¹ Delayed conduction in the form of epsilon waves in the right precordial leads, especially in the setting of a left bundle-branch VT, suggests reentry involving nonischemic-based scar of the right ventricle. Careful evaluation for ARVD/C should be performed. Ventricular tachycardia in the setting of Brugada syndrome is thought to be due to a reentrant mechanism, though research is ongoing to determine the mechanism with certainty. Any evidence for His-purkinje system disease as indexed by QRS widening, but especially in the setting of a dilated cardiomyopathy, can predispose to bundle branch reentrant ventricular tachycardia.

Clues from the 12-Lead Morphology of the Ventricular Tachycardia

A 12-lead ECG recording of VT is a critically important piece of information in evaluating and treating the patient with VT. Characteristic patterns are often observed that can localize the site of origin or exit of VT to a specific region of the heart. In addition, these recordings greatly aid the invasive treatment of VT by defining clinical and nonclinical arrhythmias induced in the EP lab and providing a rationale for pacemapping to mimic unmappable VT or VTs that are not inducible in the EP laboratory. Unfortunately, relying on specific 12-lead ECG morphologic features of ventricular tachycardia, except in very specific circumstances, to define or even narrow among the mechanistic possibilities is limited. That said, outflow tract tachycardias characterized by large monophasic R waves in the inferior leads, repetitive VPDs, or frequent nonsustained runs of an irregular tachycardia, whether arising from the RVOT or the LVOT, can confidently be attributed to triggered activity⁹ and treated accordingly. Importantly, the origin of reentrant VT associated with RV or LV cardiomyopathy can frequently originate near the peripulmonic, aortic, and superior mitral valve orifice. As such, these tachycardias will mimic morphology of outflow tract VT due to a triggered mechanism. The presence of multiple VT morphologies and the identification of a region of low bipolar voltage surrounding these valvular structures support the diagnosis of nonischemic cardiomyopathy and a probable reentrant VT mechanism. Occasionally tachycardias appear to also be of an automatic or triggered mechanism in this setting.

As indicated, a situation commonly encountered in patients with structural heart disease is the presence of more than one ventricular tachycardia morphology. In our experience, paired ventricular tachycardias with similar cycle length are frequently due to reentry involving a large circuit, as shown in Figure 1. Panels A and B in Figure 1 show two clinical VTs with similar cycle lengths but very different axis recorded from the same patient. During ablation, these VTs were found to be due to reentry involving the same scar-based circuit but entering and exiting the scar in opposite directions with components of the circuit between the exit sites confirmed using entrainment criteria (Fig. 1, panels C and D). In our experience, the combination of scar-based structural heart disease, especially of an ischemic etiology, coupled with two VTs of "opposite" axis but similar cycle length often points to macroreentry as the mechanism similar to that which is observed in right atrial flutter.

It would be a mistake to rely on cycle length stability or instability during VT as a means to assess mechanism. That is to say, regularity does not equal reentry and irregularity does not equal triggered activity or automaticity. Figure 2 illustrates an example of dramatic cycle length variability of VT occurring in the setting of a reentrant mechanism. In this figure, there is local exit block from the reentrant ventricular tachycardia circuit, resulting in abrupt halving of the surface tachycardia cycle length, while the local electrogram demonstrates the ongoing regular ventricular tachycardia. The substrate for this type of finding is extensive scarring—in this case ARVD/C—so that the entirety of the reentrant circuit is contained within the scar.



Figure 1. Panel A shows a 12-lead ECG recording of a Right Bundle Left Superior (RBLS) axis VT, CL 518 msec. Panel B shows a 12-lead ECG recording from the same patient of a Right Bundle Right Inferior (RBRI) axis VT, CL 510 msec. Panels C and D show the circuits (arrows) of the VTs from panels A and B, respectively, as defined by standard entrainment mapping during sustained VT induced in the EP lab (not shown). The circuits are superimposed on a partial LV activation map (CARTO) of the RBLS VT. Exit sites are shown by the arrows. These two paired VTs entered and exited the large macroreentrant circuit from opposite aspects.

Clues from the Initiation and Termination of VT

The initiation and/or termination of VT can have important implications for mechanism. Accelerated idioventricular tachycardia (AIVT) is an excellent example of this. Though most often observed in the setting of acute myocardial infarction and reperfusion, it can also be seen in acute myocarditis, hypertensive heart disease, digitalis intoxication, and cocaine intoxication.^{5,6} The behavior of this rhythm strongly suggests



Figure 2. This figure shows the surface ECG, distal and proximal poles of the ablation catheter recording, and RV apical recording obtained during mapping of sustained macroreentrant VT mapped to the RV free wall. Shown is a period of surface ECG and RV apical rate variability characterized by the abrupt halving of the cycle length. Catheter recording from a site of early diastolic activity (seen on the ablation catheter) demonstrated a persistent regular interval that matched the original tachycardia cycle length.

abnormal automaticity as the mechanism.¹² It often begins as a late-coupled ventricular beat at a rate just faster than the prevailing sinus rate. If either the sinus rate increases beyond the AIVT rate or the AIVT rate slows, the VT is suppressed, only to reappear if either the sinus rate slows or the AIVT rate increases.

Automatic VTs distinguish themselves from triggered and reentrant rhythms by not being reproducibly initiated with programmed stimulation. A noninvasive correlate to this is that VT observed to initiate with a specific spontaneous VPD is very unlikely to be due to automaticity, especially if this is reproducible. In fact, VTs reproducibly observed to begin with a specific VPD are very likely to be due to reentry, as the VPD interacts with the critical components of the VT circuit in a manner that initiates VT. Initiation of triggered VTs, especially exercise associated outflow tract VTs, are often influenced by rapid pacing, catecholamine infusion, or other pharmacologic manipulations that increase the intracellular concentration of cyclic AMP,^{7,11} features often employed by electrophysiologists noninvasively when evaluating patients with stress testing (Fig. 3). The initiation of reentrant VTs can also be influenced by catecholamine infusion, but the hallmark of this type of VT is its reproducible initiation with programmed stimulation, something difficult to assess noninvasively. Importantly, many slow VTs confirmed to be reentrant in mechanism demonstrate VPDs that mimic the morphology of VT and also demonstrate the first beat of the VT to mimic the morphology of the subsequent beats. It is suspected that the VPD represents a single reentrant beat. These VTs are frequently observed with an acceleration of the sinus rate, suggesting that the enhanced catecholamine



Figure 3. Outflow tract tachycardia initiation. Panel A shows salvos of nonsustained VT recorded on leads II, V2, and V5 during treadmill stress testing. Panel B was recorded during subsequent EPS of the same patient and shows the initiation of sustained VT with burst atrial pacing during isuprel infusion.

state may enhance the perpetuation of reentry when marked conduction slowing is present.

As a slightly different manifestation of initiation, we have observed that some women with idiopathic ventricular tachycardia experience exacerbation of symptoms at particular times during their menstrual cycle,¹³ a scenario unlikely to be observed with a reentry mechanism.

Clues from the Response to Pharmacologic Manipulation

With one exception, there are no predictable rules regarding the ability of specific drugs to define ventricular tachycardia mechanism. This is unfortunate as, in theory, drug testing would be an ideal noninvasive means of defining tachycardia mechanism. The prototypical example of the effects of provocative pharmacologic effects on ventricular tachycardia is repetitive monomorphic outflow tract tachycardia (also known as adenosine sensitive ventricular tachycardia).^{7,9,14} The effects of various pharmacologic and intracellular factors that modulate intracellular calcium and cyclic AMP leading to triggered activity are shown in Figure 4, adapted from Lerman *et al.*⁷ The cellular mechanism for triggered activity in this form of outflow tract tachycardia is intracellular calcium overload leading to delayed afterdepolarizations. Adenosine abolishes triggered activity VT by reducing the concentration of intracellular cAMP and thus, intracellular calcium. In our experience, adenosine has infrequently been utilized in the noninvasive evaluation of VT. This is unfortunate because it can be diagnostic and therapeutic in the appropriate circumstances. The effects of other drugs on ventricular tachycardias are less specific to any one mechanism. Verapamil affects both outflow tract tachycardias due to triggered activity as well as idiopathic forms of fascicular VT due to reentry. Class I and III antiarrhythmics and beta-blockers also do not have specific effects targeting one or another mechanism.

Ventricular Tachycardia in the Setting of Digoxin Toxicity

Ventricular tachycardia in the setting of digoxin toxicity, thought to be due to triggered activity, has long been a source of interest to electrophysiologists. Though numerous experimental animal models support triggered activity as the mechanism of VT in digitalis toxicity, the evidence in humans has been harder to obtain.¹² We were able to evaluate the mechanism of digitalis-induced VT in 2 patients after the administration of Fab fragment.⁸ Figure 5A (two leads) and B (12 leads) show surface ECG recordings from 2 patients with sustained ventricular tachycardia in the setting of digoxin toxicity. Both patients received Fab fragments to bind Digoxin



Factors Influencing Cyclic AMP Mediated Intracellular Ca⁺⁺ Accumulation or Effecting Calcium Conductance

Figure 4. Schematic of various pharmacologic and endogenous factors affecting intracellular cyclic AMP and calcium concentration capable of modulating ventricular tachycardia due to triggered activity (adapted from Lerman et al.7).





Figure 5. Two patients with ventricular tachycardia were given Fab fragments and observed with continuous ECG monitoring. (A) Two ECG leads showing bidirectional VT in patient 1, (B) fascicular VT in patient 2, (C) resetting curves of the response to spontaneously occurring VPDs during slowing of VT, and (D) summary of findings observed in these 2 patients.

under continuous ECG monitoring. Figure 5C shows the resetting curves in response to variably coupled spontaneously arising VPDs occurring as the ventricular tachycardia slowed in response to the Fab administration. Figure 5D summarizes the findings observed in these 2 patients. In their totality, these findings point to triggered activity as the mechanism of ventricular tachycardia in digitalis-induced

TABLE 1

The Degree to Which Specific ECG Clues Support Each of the Three VT Mechanisms (See Text for Detailed Descriptions of Each ECG Clue)

	Automaticity	Triggered	Reentry
SR ECG			
Normal	++	++	+
Infract pattern	0	0	++
Brugada ECG pattern	0	0	+
Long QT	0	++	0
ARVD/CM	0	0	++
BBB	0	0	+
ECG of VT(s)			
Regular rate	0	0	+
Irregular rate	++	+	0
Outflow tract morphology	0	++	+
Paired VT morphologies	0	0	++
>1 VT morphology	0	+	++
Initiation/Termination			
Initiates with same VPD	++	+	+
Exercise testing initiates	+	++	+
Termination with adenosine	+ (transient)	++	0
VT in the setting of digoxin toxicity	0	++	0

0 = does not lend support for or against this mechanism; + = supports this mechanism; ++ = strongly supports this mechanism.

VT. These findings also provide an elegant example of how multiple spontaneous changes and perturbations during ongoing ventricular tachycardia can, based simply on careful analysis of surface ECG findings, be used to elucidate and define the mechanism of ventricular tachycardia.

Table 1 summarizes the ECG clues and features described above with regard to the degree to which they support each of the three VT mechanisms.

Future Directions

Because of the importance of understanding the mechanism of any given patient's ventricular tachycardia, research must continue to define the ways in which this can be determined. The 12-lead ECG, vitally important for understanding ventricular tachycardia, is limited with regard to its ability to define VT mechanism. Noninvasive and invasive means of determining mechanism all are in need of further research. Potentially fruitful lines of research include ongoing study of the relationship of the baseline ECG to the VT morphology in the presence or absence of structural abnormalities as assessed by echocardiography, CT imaging, and MRI imaging. Given the importance of initiation and termination with regard to VT mechanism, research involving intracardiac electrograms recorded on ICDs, especially with regard to timing and morphology of initiating VPDs, may provide fruitful avenues for understanding clinically relevant VTs.15 In our opinion, further study is warranted with regard to the effect of provocative noninvasive maneuvers (using new and old drugs, stress testing) on sustained VT to elucidate the mechanism.

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