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Review

Noninvasive clues for diagnosing ventricular tachycardia mechanism☆,☆☆

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ABSTRACT

The electrophysiologic mechanisms responsible for the initiation and maintenance of ventricular tachycardia (VT) include enhanced automaticity, triggered activity and reentry. Differentiating between these three mechanisms can be challenging for the clinician and usually requires an invasive electrophysiology study. Establishing the underlying VT mechanism in a particular patient is helpful to define the optimal therapeutic approach, including the selection of pharmacologic agents or delineation of an ablation strategy. The purpose of this review is to provide insight into the possible VT mechanisms based on noninvasive clues from the clinical history, 12-lead electrocardiogram, tachycardia onset and termination and the response to pharmacologic manipulation.

Introduction

The electrophysiologic mechanisms responsible for ventricular tachycardia (VT) fall in one of 3 categories: [1] abnormal automaticity; [2] triggered activity; and [3] reentry [1]. (See Tables 1 and 2.)

Understanding the cellular mechanism of VT in a particular patient is relevant for the prognosis, pharmacological management and also to define the optimal mapping and ablation strategies. Most focal VTs, due to a triggered or automatic mechanism, are amenable to betablockade therapy. In contrast, reentrant VTs usually require membrane active antiarrhythmic agents that slow conduction or prolong refractoriness to prevent reentry. In focal VTs the 12-lead electrocardiogram (ECG) provides a powerful tool for localizing the focal origin and the target for ablative therapy. In reentrant VTs the 12-lead ECG may only identify an exit for a larger macro-reentrant circuit. Activation mapping to define the site of earliest ventricular activation is the mainstay for mapping of focal VTs, typically complemented with pacemapping. On the other side, macro-reentrant VTs are better mapped with a combination of voltage mapping to delineate the arrhythmogenic substrate and entrainment maneuvers to define the critical components of the circuit. Focal VTs can be ablated with a single ablation lesion, whereas macro-reentrant VTs require linear lesions between unexcitable boundaries aimed at interrupting the width of the reentrant circuit.

Correct identification of the mechanism can be difficult in clinical practice and the 12-lead ECG by itself is limited for this purpose [2]. In this article we review some noninvasive clues from the clinical history, 12-lead ECG, telemetry monitoring or response to pharmacologic agents that may help the clinician to recognize the potential VT mechanism.

Pathophysiology

Abnormal automaticity

Automaticity is the property of cardiac cells to generate spontaneous action potentials and is the result of diastolic depolarization caused by a net inward current during phase 4 of the action potential [3]. Normal automaticity is a property of the sinoatrial and atrioventricular nodes and depends mainly on 2 phenomena: [1] diastolic activation of I_f (funny current), a mixed Na-K inward current, which unlike most voltage-sensitive currents, is activated by hyperpolarization rather than depolarization; and [2] release of calcium from the sarcoplasmic reticulum into the cytosol. The calcium, in turn, activates the Na^+-Ca^{2+} exchanger, resulting in a net influx of sodium ions [4].

Ventricular myocardial cells do not display spontaneous diastolic depolarization or automaticity under normal conditions, but abnormal automaticity may occur under pathological conditions when the resting membrane potential becomes less negative. This may be consequence of a decrease in I_{K1} or an enhanced calcium release from the sarcoplasmic reticulum [4,5]. Similar to normal automaticity, abnormal automaticity is enhanced by β-adrenergic agonists and by reduction of external potassium.

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Table 1
Electrophysiologic maneuvers for diagnosis of VT mechanism.

	Automaticity	Triggered activity	Reentry
Initiation with PES	No	Sometimes	Yes
Termination with PES	No	Sometimes	Yes
Reset with fusion	No	No	Yes
Entrainment with fusion	No	No	Yes
Response to overdrive pacing	Suppression	Acceleration/termination	Entrainment/termination
Response to ventricular extrastimuli	Resetting with flat response	Resetting with flat/decreasing response	Resetting with flat/increasing/mixed response

Examples of abnormal automaticity include accelerated idioventricular rhythm in the setting of acute ischemia, myocarditis or cocaine intoxication [6,7].

Triggered activity

It refers to action potential formation resulting from oscillations in membrane potential that are dependent on the preceding action potential (Fig. 1). When the amplitude of one of these afterdepolarizations reaches certain threshold, voltage-gated ion channels are activated, generating an action potential. Triggered activity can occur in the form of early or delayed afterdepolarizations. Early afterdepolarizations (EADs) occur during phase 2 or 3 of the cardiac action potential and are more manifest at slower heart rates, whereas delayed afterdepolarizations (DADs) occur during phase 4 of the action potential, after full repolarization, and are more dependent on faster heart rates.

Examples of EADs include drug and electrolyte-induced Torsades de Pointes and some forms of polymorphic VT due to congenital long QT syndrome [8,9]. DADs are responsible for the majority of outflow tract VTs, catecholaminergic polymorphic ventricular tachycardia (CPVT) and ventricular arrhythmias associated with digitalis toxicity [10–14].

Reentry

It is the most common mechanism of VT. It involves continuous repetitive propagation of an impulse around an area of anatomical or functional conduction block (Fig. 2). The following 3 criteria were originally proposed by Mines for identification of reentry: 1) unidirectional block must occur; 2) a region of slow conduction with return of the excitatory wave to its point of origin; and 3) interruption of the reentrant circuit at any points should terminate the tachycardia [15]. The substrate for reentry requires the presence of 2 pathways with different electrophysiologic properties separated by a central area of block (anatomical or functional). When an impulse encounters the central obstacle, unidirectional block occurs in one of the pathways and slow conduction occurs through the other pathway, creating a circus movement. For reentry to occur, the conduction within the unblocked pathway must be slow enough so the previously blocked pathway can recover its excitability by the time the reentrant wavefront returns. In other words, the anatomical length of the circuit should equal or exceed the reentrant wavelength.

Reentrant arrhythmias can be reproducibly initiated and terminated by programmed stimulation. They can also interact with pacing and demonstrate the hallmark features of resetting and entrainment with fusion [16,17]. Resetting is the advancement of a tachycardia impulse by timed premature electrical stimuli. The extrastimulus is followed by an interval that is less than a fully compensatory pause before resumption of the original rhythm. Entrainment is the continuous resetting of a tachycardia circuit. During overdrive pacing the tachycardia is accelerated to the pacing rate, with resumption of the intrinsic rate upon abrupt cessation of pacing.

Examples of reentry include: 1) scar-related VT in patients with structurally abnormal hearts due to ischemic or nonischemic cardiomyopathies; 2) bundle branch reentry, which is typically seen in patients with infrahisian conduction disease and involves antegrade conduction over the right bundle and retrograde conduction over the left bundle (or vice versa); 3) idiopathic left ventricular tachycardia (also known as fascicular VT, Belhassen VT or verapamil-sensitive VT), in which the macro-reentrant circuit involves the left posterior fascicle (or less commonly the left anterior fascicle) and abnormal slowly conducting Purkinje fibers; and 5) Phase 2 reentry associated with VAs in Brugada syndrome.

Table 2
Noninvasive clues for diagnosis of VT mechanism.

	Automaticity	Triggered activity	Reentry
Normal ECG	++	++	+
Abnormal ECG (Q waves, epsilon waves, BBB)	0	0	+
Outflow tract morphology	0	++	+
Warm up/cool down	+	−	−
Morphology of first beat	Identical to subsequent	Identical to subsequent	Often different to subsequent
Initiation during exercise	+	++	+
>1 VT morphology	−	−	+
Paired VT morphologies	−	−	+
Adenosine	Slowing or transient termination	Termination	No effect
Catecholamine facilitation	Increase	Increase	Increase/decrease

Sinus rhythm ECG

Baseline sinus rhythm 12-lead ECG may be helpful by indicating disease processes known to be associated with specific VT mechanisms. The presence of Q waves consistent with prior myocardial infarction indicates the substrate for scar-related reentry, especially if the VT morphology is consistent with an exit from the region of the infarct. Epsilon waves in the right precordial leads, especially in the setting of a left bundle-branch block VT, is a marker of arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D) and suggests reentry involving non-ischemic scar localized to the right ventricle. Any evidence for His-Purkinje system disease as indexed by QRS widening, especially in the setting of a dilated cardiomyopathy, can predispose to bundle branch reentrant VT. A Brugada pattern is associated with phase 2 reentry, a special type of reentry proposed to be caused by heterogeneity in action potential distribution between the epicardium and endocardium [18].

A normal baseline ECG often reflects a structurally normal heart. Although VT due to any of the 3 mechanisms can occur in patients without structural heart disease, a normal baseline ECG coupled with specific morphologic patterns of VT may indicate a most likely mechanism: triggered activity for outflow tract tachycardias [12,13] and reentry involving the Purkinje system in fascicular VT [19].

Twelve-lead morphology of the ventricular tachycardia

A 12-lead ECG recording of the VT allows to localize the site of origin or exit to a discrete region of the heart, however its value to define the VT mechanism is limited. Having said that, certain ECG patterns are