JACC: CLINICAL ELECTROPHYSIOLOGY VOL. ■, NO. ■, 2018

PUBLISHED BY ELSEVIER

Infarct-Related Ventricular Tachycardia: Redefining the Electrophysiological Substrate of the Isthmus During Sinus Rhythm

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ABSTRACT

OBJECTIVE In this study, the scientific objective was to characterize the electrophysiological substrate of the ventricular tachycardia (VT) isthmus during sinus rhythm.

BACKGROUND The authors have recently described the electrophysiological characteristics of the VT isthmus using a novel in vivo high-resolution mapping technology.

METHODS Sixteen swine with healed infarction were studied using high-resolution mapping technology (Rhythmia, Boston Scientific, Cambridge, Massachusetts) in a closed-chest model. The left ventricle was mapped during sinus rhythm and analyzed for activation, conduction velocity, electrogram shape, and amplitude. Twenty-four VTs allowed detailed mapping of the common-channel "isthmus," including the "critical zone." This was defined as the zone of maximal conduction velocity slowing in the circuit, often occurring at entrance and exit from the isthmus caused by rapid angular change in activation vectors.

RESULTS The VT isthmus corresponded to sites displaying steep activation gradient (SAG) during sinus rhythm with conduction velocity slowing of 58.5 ± 22.4% (positive predictive value [PPV] 60%). The VT critical zone displayed SAG with greater conduction velocity slowing of 68.6 ± 18.2% (PPV 70%). Critical-zone sites were consistently localized in areas with bipolar voltage ≤0.55 mV, whereas isthmus sites were localized in areas with variable voltage amplitude (1.05 ± 0.80 mV [0.03 to 2.88 mV]). Importantly, critical zones served as common-site "anchors" for multiple VT configurations and cycle lengths. Isthmus and critical-zone sites occupied only 18.0 ± 7.0% of the low-voltage area (≤1.50 mV). Isolated late potentials were present in both isthmus and nonisthmus sites, including dead-end pathways (PPV 36%; 95% confidence interval: 34.2% to 39.6%).

CONCLUSIONS The VT critical zone corresponds to a location characterized by SAG and very low voltage amplitude during sinus rhythm. Thus, it allows identification of a re-entry anchor with high sensitivity and specificity. By contrast, voltage and electrogram characteristics during sinus rhythm have limited specificity for identifying the VT isthmus. (J Am Coll Cardiol EP 2018;■:■-■) © 2018 by the American College of Cardiology Foundation.

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All authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the *JACC: Clinical Electrophysiology* author instructions page.

Manuscript received March 9, 2018; revised manuscript received April 19, 2018, accepted April 26, 2018.

ISSN 2405-500X/$36.00 https://doi.org/10.1016/j.jacep.2018.04.007

ABBREVIATIONS AND ACRONYMS

EGM = electrogram

LAVA = local abnormal ventricular activity

LV = left ventricle

NPV = negative predictive value

PPV = positive predictive value

RVA = right ventricular apex

SAG = steep activation gradient

VT = ventricular tachycardia

Activation mapping of ventricular tachycardia (VT) is the gold-standard method for description of the re-entrant circuit and identification of its isthmus. However, activation mapping is limited by hemodynamic nontolerance and relatively low temporal and spatial resolution. Substrate mapping has been used as an alternative method to identify the isthmus of post-infarction VT during sinus rhythm (1-6). The principle underlying substrate mapping is that bundles of surviving myocytes within heterogeneous scar identified during sinus rhythm may form isthmuses during VT. This has led to the widespread use of voltage mapping to identify channels of viable myocardium, pace-mapping techniques aimed to produce a QRS morphology similar to the VT, and identification of abnormal electrograms (EGMs) (i.e., fractionated, late potentials) thought to represent the VT isthmus (7,8). Despite this approach, current substrate-mapping techniques have limited specificity for identifying the VT isthmus during sinus rhythm (9). It is therefore not surprising that confined ablation strategies guided by current substrate mapping techniques are less effective than extensive ablation strategies directed in eliminating all viable myocardium in and around the infarct (i.e., substrate homogenization) (10-15). This underlies the limitations of current substrate-mapping techniques to specifically identify the electrophysiologic substrate: the specific zone(s) in and around the infarct, capable of supporting re-entry and VT.

A major limitation of current substrate-mapping techniques relates to oversimplification of the relationship between the VT circuit and the underlying substrate. In particular, it assumes that the substrate for re-entry in patients with healed infarction is purely structural, neglecting the electrophysiological properties responsible for initiation and perpetuation of re-entry. These have been studied in detail and include slow conduction due to cellular uncoupling and nonuniform anisotropic conduction and dispersion of refractoriness with nonuniform recovery of excitability (16). Fundamental work in a canine model of healed infarction showed that isthmuses of different VTs often share one common region and that this region can be identified during sinus rhythm as an area with steep conduction slowing (17). However, these studies required detailed EGM recordings from a multielectrode array placed on the epicardial surface, limiting its applicability to humans.

Recent advancements in mapping technology approved for use in human provide an opportunity to examine the electrophysiological properties of VT in greater detail. We have recently described the electrophysiological properties of the post-infarction VT circuit using high-resolution mapping technology (Rhythmia, Boston Scientific, Marlborough, Massachusetts) (18). In this report, we describe the structural and functional properties of the VT isthmus during sinus rhythm. In particular, we compare these properties to non-isthmus sites in attempt to better characterize the *arrhythmogenic substrate* of infarct-related VT.

METHODS

SWINE INFARCT MODEL. We studied 16 swine with chronic anterior wall infarction. Our swine model has been described previously and closely approximates human infarction with re-entrant VT (19). In brief, Yorkshire swine (male, 35 kg to 40 kg) underwent selective balloon occlusion of the left anterior descending artery for duration of 180 min. After 8 to 10 weeks, animals underwent electrophysiology study, including mapping during sinus rhythm and VT, as described subsequently. This research was performed at the Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts. The Institutional Animal Care and Use Committee approved this research protocol.

ELECTROPHYSIOLOGY STUDY. The electrophysiology study was performed under general anesthesia with isoflurane inhalation. A pentapolar catheter (Bard EP, Lowell, Massachusetts) was placed in the right ventricular apex (RVA) to allow pacing and to act as an intracardiac activation reference. The proximal electrode was positioned in the inferior vena cava and served as an indifferent unipolar electrode. The left ventricle (LV) was initially mapped during sinus rhythm and then during VT as described subsequently. Induction of VT was performed using programmed stimulation from the RVA at a current strength twice the capture threshold and a pulse width of 2.0 ms. Stimulation was performed at paced cycle lengths of 600 and 400 ms with 1 to 4 extrastimuli down to ventricular effective refractory period. If electrical stimulation from the RVA failed to induce VT, stimulation was repeated from the right ventricular outflow tract, followed by the LV. We attempted to map all sustained monomorphic VTs. If the VT was not hemodynamically tolerated, it was terminated by pacing or electrical cardioversion. In these cases, vasopressor support (phenylephrine