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Authors

Bradfield, Jason S
Shivkumar, Kalyanam

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Cardiac Resynchronization Therapy–Induced Proarrhythmia: Understanding Preferential Conduction Within Myocardial Scars

Jason S. Bradfield, MD and Kalyanam Shivkumar, MD, PhD

UCLA Cardiac Arrhythmia Center, UCLA Health System, Los Angeles, CA

Abstract

Cardiac resynchronization therapy (CRT)–induced proarrhythmia is a clinically described entity, often included in the differential diagnosis for patients presenting with electrical storm, but rarely proven based on available data. Electrophysiologists consulting on patients with a CRT device in place often query the possibility of this entity. Yet, unless electrical storm immediately follows CRT implantation and the ventricular tachycardia (VT) morphology matches the left ventricular (LV) pacing morphology, the speculation is often short-lived.

Keywords

Editorials; ablation; proarrhythmia; ventricular tachycardia

Understanding of this clinical entity is complex, as the factors controlling VT initiation and maintenance when pacing within or near scar are multi-factorial, incompletely understood, and likely variable based on several factors including local electroanatomic parameters as well as complex autonomic modulation. Furthermore, myocardial scars are known to progress over time, and cardiac impulses can have variable entrances and exits from a scar, which can complicate time of presentation and ECG interpretation in an individual patient.

Current Study

In the current study, Roque et al¹ present their data on CRT-induced proarrhythmia because of pacing from within, or adjacent to, an epicardial scar demonstrated on cardiac MRI (cMRI). The authors demonstrate that this phenomenon can be successfully managed with catheter ablation and that in most cases CRT can be restored after ablation.

The authors should be congratulated on the most comprehensive evidence to date on this topic. They undertook meticulous mapping of the endocardium and epicardium in the majority of patients studied. CRT-induced proarrhythmia patients were more likely (62%) to have nonischemic cardiomyopathy (NICM) and more likely to present with electrical storm,

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Correspondence to Kalyanam Shivkumar, MD, PhD, UCLA Cardiac Arrhythmia Center, UCLA Health System, David Geffen School of Medicine at UCLA, 100 UCLA Medical Plaza, Suite 660, Los Angeles, CA 90095-1679. KShivkumar@mednet.ucla.edu.

Disclosures

None.

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as well as heart failure/cardiogenic shock. One would assume the increased propensity for heart failure/cardiogenic shock was directly related to the electrical storm induced by CRT as well as the associated lack of successful resynchronization.

However, what is the mechanism for the increased risk of electrical storm? Increased dispersion of repolarization has been described in CRT patients and potentially predicts risk of appropriate therapy.² Yet, pacing near a critical site of slow conduction, as postulated in the current article, seems to be a more important predictor of events and certainly more likely to induce monomorphic VT as apposed to polymorphic VT, as was found in this study.

It is somewhat surprising that given the ablation of critical regions of slow conduction and late potentials in this study that the pacing thresholds of these leads did not increase significantly. One would suspect that aggressive ablation in the region of the LV lead might limit future exit of paced impulses from the scar, similar to the way ablation limited induction of VT. On the contrary, the authors demonstrate that despite the theoretical risk, epicardial ablation can be done safely and effectively, with promising outcomes and a high likelihood of allowing reinitiation of CRT. It is possible that the increased pacing options with increased electrode spacing of the quadrapolar lead that was frequently used in this series may have decreased the chance that ablation led to pacing failure. It is also possible, however, that pacing from widely spaced electrodes has increased potential to capture a preferential highway of slow conduction and induce VT. Regardless of the lead used, this finding reinforces the belief that within any scar there are many 3-dimensional highways for electric conduction during sinus rhythm or pacing and further raises the question of why one such highway is preferred for VT induction and perpetuation.

Although providing important information, the current study does have limitations. One limitation is that of the 8 patients that met criteria for CRT-induced proarrhythmia, only 60% had clear correlation between the lead position and a documented epicardial scar. Therefore, the mechanism may be somewhat different in the 2 groups of patients, those pacing within scar and those pacing adjacent to a scar. Furthermore, the authors do not provide detailed data regarding pacing and VT morphologies. This is important to determine whether the impulse exit from the scar during pacing and VT is similar, or if more than one potential exit is present.

Pacing within scar, presumably at or near a critical isthmus, is expected to be proarrhythmic. With regards to mechanism, the authors describe what is the equivalent to a pace-map induction of VT during substrate mapping.³ However, additional potentially important clinical parameters related to LV lead pacing, or pacing adjacent to said lead, including stim-QRS latency⁴ are not reported. Unfortunately, we do not know the true prevalence of proarrhythmia for LV lead pacing from within scar, as the number of CRT patients with an LV lead within scar that are VT free is not reported in the current study and not known from larger cohorts. How these patients' scars differ from those with proarrhythmia requires further study.

Pacing from a site near, but not within, the critical region of slow conduction causing electrical storm is more difficult to understand. Rarely during a VT ablation procedure do we see straight pacing at a slow heart rate (base rate of CRT) induce sustained VT. Typically, extrastimulus testing is required when pacing from outside the scar to induce reentrant arrhythmias. This raises the importance of further research to better understand scar characteristics and behavior.

The use of epicardial unipolar scar to define an anatomic lead-scar relationship also raises interesting questions. Unipolar epicardial scar without local bipolar scar suggests distant scar in the mid- or endocardial region.⁵ However, the use of unipolar voltage to predict distant scar has only been validated to date with endocardial mapping to predict mid- or epicardial scar presence. There was no correlation with endocardial bipolar scar in this study. Furthermore, endocardial unipolar findings did not predict proarrhythmia, and 35% of patients without CRT-proarrhythmia had abnormal endocardial unipolar findings in the region of the LV lead.

Interpretation and Future Direction

The current article answers many important questions and points to many interesting directions for future research:

1. Are NICM patients at increased risk for this phenomenon given reported propensity for epicardial scars, and should this lead to more aggressive preoperative imaging in NICM patients?
2. Can we better understand the characteristics of a scar that control electric propagation, and will a combination of electroanatomic and imaging criteria provide the answer?
3. Is the presence of scar sufficient to avoid placing LV leads in the associated region or are there specific scar characteristics that can be delineated and are more high risk for lead placement? Can these characteristics eventually be ascertained with cMRI or other imaging modalities?

Epicardial scar is most commonly described in NICM, however can be seen in ischemic cardiomyopathy. Therefore, the risk of this phenomenon is not likely to be limited to the NICM population and deserves careful consideration in all patients referred for CRT. Furthermore, if patients with distant scar on the mid-myocardium or apposing surface are prone to CRT-induced proarrhythmia, then epicardial scar may not be a prerequisite for this phenomenon, making it difficult to withhold CRT therapy based on MRI findings.

Patients with ischemic and NICM have complex electroanatomic substrates. Discrete myocardial scars, microfibrosis, and inflammation can be present. These abnormalities may involve the endocardial, mid-myocardial, and epicardial regions, forming a complex 3-dimensional substrate for VT. Further complicating the picture is the interplay between dense scar, border zone tissue, and interspersed normal tissue,⁶ which lead to regions of slow conduction that potentially allow re-entry to occur. However, characteristics that

differentiate preferential paths of conduction within scar from paths that do not support reentrant VT have limited data in the literature.^{4,7-12}

Electrophysiological parameters found during an invasive study such as slower conduction velocity, longer stim-QRS latency, and late potentials during sinus or paced rhythm, as well as entrainment of hemodynamically tolerated VT, can help localize potential regions of slow conduction. However, not all regions with late potentials or long stim-latency will support VT,¹³ and these parameters focus on characteristics of critical regions of slow conduction deep within scar. Therefore, these parameters have limitations and even less is known about the factors that control impulse entrance into, or exit from, the border zone itself, forming a functional line-of-control.

From a practical perspective, cMRI with image overlay of the coronary veins can help differentiate which patients might be appropriate candidates for a transvenous LV lead placement by assessing the venous anatomy in relationship to any associated scar. Alternatively, a surgical approach can be considered if no candidate vessels are present. Furthermore, overlay of the phrenic nerve may help predict sites safely removed from risk of phrenic capture. In the past, there has been concern on use of cMRI in patients with implantable cardioverter-defibrillators because of risk of device malfunction and as a result of poor image quality of the LV lateral wall due to generator artifact. Recent data demonstrate that cMRI can be done safely in most patients without abandoned leads, and now artifact can be successfully minimized with new wideband technology.^{14,15} Therefore, even in patients who require upgrade to CRT from a previously paced implantable cardioverter-defibrillator, scar assessment based on delayed enhancement can be accomplished safely and with quality imaging.

Conclusions

CRT-induced proarrhythmia is an important clinical entity that needs to be considered in the care of patients with VT and CRT devices, as well as when a new CRT system implant is contemplated. The authors have demonstrated that ablation can play a role in allowing return to CRT in these patients. However, many more patients have scar at or near a CRT LV lead then actually have CRT-induced proarrhythmia. Therefore, there are clearly characteristics of specific scars that predispose to proarrhythmia. The utility of cMRI continues to grow for preprocedure imaging in patients with cardiomyopathy and VT, but the ability of cMRI to risk stratify the arrhythmogenicity of pacing within or near a given scar is still limited and will be an important area for further research.

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