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EDITORIAL COMMENT

Connecting the Dots

The Relevance of Scar in Nonischemic Cardiomyopathy*

Alan H. Kadish, MD, Jason C. Rubenstein, MD
Chicago, Illinois

Delayed-enhancement magnetic resonance imaging (DE-MRI) has emerged as the gold standard imaging technique for defining myocardial scar with high resolution. Gadolinium contrast washes out of the blood pool and accumulates in the extracellular space. Tissues with weak intracellular bonds and high amounts of noncellular space, such as necrotic tissue or fibrous scar, will develop higher concentrations of this magnetic resonance imaging (MRI) contrast agent than will healthy tissues. Scar detected by DE-MRI has been shown to closely match histologically proven myocardial infarction (MI) (1). After an MI, cardiac myocytes become necrotic and cause an inflammatory response that initiates fibroblast replication, which replaces the necrotic tissue with noncellular collagen. This myocardial scar formation leads to cardiac dysfunction and ischemic cardiomyopathy. The DE-MRI has shown prognostic value after MI for viability (1,2), functional recovery after MI (2), ventricular arrhythmia (3), and long-term mortality (4). Delayed enhancement has been shown to correlate with areas of low voltage on electroanatomic mapping (5), and can define critical targets of VT circuits during ablation in patients with prior myocardial infarction (6). Presumably the presence of scar, and in particular the border zone between scar and normal myocardium, allows re-entrant circuits to form.

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Myocardial scar has also been detected by DE-MRI in patients with nonischemic cardiomyopathy. The mechanism of scar formation in patients with nonischemic cardiomyopathy is not clear because neither obstructive coronary disease nor clinical ischemia is typically seen. Yet over one-half of these patients also show macroscopic evidence of cardiac tissue replacement with fibrous tissue. The regions of scarring may be different in these 2 disease processes; ischemia leads to a predominately endocardial scar that may be transmural, whereas scar in nonischemic cardiomyopathies tends to be isolated to the midwall or epicardium. In contrast to the studies establishing the utility of DE-MRI in ischemic cardiomyopathy, fewer data are available on the clinical utility of DE-MRI in the nonischemic population. A DE-MRI can differentiate ischemic from nonischemic cardiomyopathies based on enhancement patterns (7). The presence of enhancement has been shown to be predictive of higher mortality as well as ventricular arrhythmia, even in the absence of coronary disease or infarction (8). In nonischemic patients with monomorphic ventricular tachycardia (VT), basal scar has been associated with arrhythmia (9). However, prior studies have not clearly established that VTs are related to DE-MRI scar in patients without coronary disease, as has been shown in patients with healed infarction.

One challenge in catheter ablation of VT, especially in the setting of nonischemic cardiomyopathy, is that origin of VT is more often intramural or epicardial than it is in patients with coronary artery disease. Prior studies have examined the use of surface QRS configuration in an attempt to distinguish endocardial, midmyocardial, and epicardial origins of VT. Despite some encouraging preliminary results, algorithms in patients with nonischemic cardiomyopathy that utilize surface electrocardiogram only have not proven to be highly accurate (10). An additional technique to direct the site of origin for VT ablation before performing catheter ablation would be useful. Also, monomorphic VT is often not reproducibly inducible in patients with nonischemic dilated cardiomyopathy, and thus a nonmapping technique that can distinguish the site of origin of VT remains attractive.

In this issue of the *Journal*, Bogun et al. (11) provide further compelling evidence showing that myocardial scarring, as identified by DE-MRI, is associated with ventricular arrhythmias and extends this observation to patients with nonischemic cardiomyopathy. They also suggest that scar location can be a helpful guide to ablation. The study population consisted of 29 patients with nonischemic cardiomyopathy who had been referred for catheter ablation because of either VT (n = 9) or symptomatic premature ventricular complexes (n = 20). Little information is provided about other comorbid diseases, but the average ejection fraction was 39%. Scar was classified as either endocardial, epicardial, intramural, or transmural, and scar volumes were quantified. Bogun et al. (11) showed that although 48% of the study population had scar by DE-MRI, all patients referred for sustained VT had some evidence of scar. In those patients in whom a critical site of VT was identified, it occurred within areas of scar in all cases (11). In patients with predominantly intramural delayed enhancement, catheter ablation was uniformly ineffective. Two patients had DE-MRI scar limited to the epicardial surface; neither of these patients had VTs that

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From the Cardiovascular Clinical Trials Unit and the Division of Cardiology, Feinberg School of Medicine, Northwestern University, Chicago, Illinois. Supported in part by a grant from St. Jude's Cardiac Rhythm Management Division and a grant from the National Heart, Lung, and Blood Institute (R01 HL091069).

could be ablated from the endocardium. In contrast, in patients who had predominantly endocardial enhancement, 71% underwent successful catheter ablation of all VTs via an endocardial approach; the remaining 29% had a majority of VTs eliminated. In the entire cohort, there were 66 targeted arrhythmias, of which 36 (55%) were successfully ablated.

The primary finding of this study is that DE-MRI enhancement can be used as a guide for VT and premature ventricular complex ablation, even in patients considered to have nonischemic cardiomyopathies. There are 2 potentially important implications. This finding could have important significance for planning invasive electrophysiologic interventions. In addition, the results of this study further reinforce the concept that scar burden by DE-MRI may be correlated with the incidence of ventricular tachyarrhythmia. Further studies are needed to define the role that DE-MRI may have in noninvasive risk prediction of sudden cardiac death, in both the ischemic and the nonischemic cardiomyopathy populations.

Some limitations of the study should be noted. Only 29 patients were included in the study. Only 2 had scar confined to the epicardial surface. Thus, the observations made in this patient population are extremely preliminary. The number of patients with intramural scar was also limited. Given the inaccuracies of registering MRI images to electroanatomic maps (almost 5 mm in this study) and the resolution of DE-MRI images (1.4 mm in-plane, 8 mm out-of-plane), it seems unlikely that the current technologies can be used to guide specific lesion delivery or identify the critical sites of ablation. Nonetheless, the results of the study by Bogun et al. (11) suggest that DE-MRI may be a useful technique in patients with VT and nonischemic cardiomyopathy.

Although not completely conclusive because of small patient number, the results of this study suggest that scar location, identified by DE-MRI before a catheter ablation procedure, may help localize sites for effective ablation. An endocardial approach, epicardial approach, or continued trials of medical therapy may be appropriate depending on scar location. The data in this article seem strongest for the ability of DE-MRI to distinguish between endocardial and nonendocardial sites of VT origin. If these findings are confirmed in a larger patient population, scar localization could represent an important adjunct of catheter ablation in nonischemic dilated cardiomyopathy. This study also gives hope that in the near-future DE-MRI image integration in the electrophysiology laboratory will be a major component of VT ablation navigation.

Reprint requests and correspondence: Dr. Alan H. Kadish, 251 East Huron, Feinberg Pavilion, Suite 8-536, Chicago, Illinois 60611. E-mail: a-kadish@northwestern.edu.

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