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EDITORIAL COMMENT

CMR–Guided Targeting of Gaps After Initial Pulmonary Vein Isolation*

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Pulmonary vein (PV) isolation has become an established treatment for symptomatic drug-refractory atrial fibrillation (AF). However, the efficacy of AF ablation is suboptimal, with a majority of failures resulting from discontinuities in circumferential ablation sets for PV isolation. The presence of PV entrance and exit conduction block serves as a surrogate of complete circumferential ablation of the PV ostium. Action potential duration, amplitude, and conduction time are acutely reduced in tissues within 2.5 mm of ablation lesions. However, these electrophysiological changes of surrounding myocardium are transient and resolve within 4 weeks of lesion formation (1). Impairment of conductivity may lead to misidentification of gaps as ablated tissue, with subsequent full recovery of conduction over time. The use of surrogates of complete ablation, including persistence of conduction block with adenosine administration and lack of pacing capture on ablated tissue, improvement outcomes, but recurrences and gaps continue to be observed. Imaging of gaps in circumferential ablation sets may be possible using endoscopy, intracardiac ultrasound, and optical coherence tomography (2–4). These techniques offer relative simplicity of hardware incorporation into electrophysiology laboratories, but are limited by the need for specific orientation of the catheter-tissue interface to appropriately visualize lesions.

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In this issue of *iJACC*, Bisbal et al. (5) evaluated the utility of late gadolinium-enhanced (LGE) cardiac magnetic resonance (CMR) at 3-T for targeting gaps during repeat AF ablation in 15 patients. The extent and distribution of fibrosis was estimated using a signal intensity map with thresholds at 40 ± 5% and 60 ± 5% of maximum intensity. The intensity map was then projected onto a 3-dimensional left atrial reconstruction and imported into the mapping system. Endocardial mapping identified 49 PVs with electrical reconnection. All 49 veins showed evidence of incomplete PV isolation by CMR. In contrast, endocardial mapping identified 7 PVs with persistent electrical isolation. Of these 7 PVs, 3 showed gaps on CMR and 4 had complete isolation according to CMR. The site of electrical reconnection matched with a gap detected by CMR in 79% of 18 PVs with reliable circular catheter mapping. Although procedural duration or fluoroscopy times were not different in the study groups, guidance by LGE CMR was associated with reduction of ablation duration.

Using the values listed in **Table 1**, the diagnostic test performance for identification of reconnected PVs by CMR can be summarized as follows: sensitivity 100% (95% confidence interval [CI]: 93% to 100%), specificity 57% (95% CI: 19% to 90%), positive likelihood ratio 2.3 (95% CI: 1.0 to 5.5), and negative likelihood ratio 0. Because the prevalence of PV reconnections in this cohort was high (87.5%), the diagnostic indexes performed superbly, with a positive predictive value of 94% (95% CI: 84% to 99%) and negative predictive value of 100% (95% CI: 40% to 100%). It is important to note, however, that if we assume constant sensitivity and specificity, a lower PV reconnection prevalence would significantly diminish the performance of CMR. For example,

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TABLE 1 Diagnostic Performance of Cardiac Magnetic Resonance for Detection of Conduction Gaps

	Cardiac Magnetic Resonance		
Electroanatomic Mapping	Gap Present	Gap Absent	Totals
Gap Present	49	0	49
Gap Absent	3	4	7
Totals	52	4	56

if the prevalence of PV reconnection was reduced to 40%, the same sensitivity and specificity measures would yield a positive predictive value of 61%. Minor study limitations include the fact that comparisons of procedure, ablation, and fluoroscopy duration were made in a nonrandomized cohort consisting of the 15 patients assigned to image guidance and 15 patients who underwent conventional procedures. The lack of randomization may have introduced bias if radiofrequency times were different due to other clinical differences between the 2 groups. In addition, the site of earliest activation by electrical mapping was compared to CMR in only 37% of PVs. Nevertheless, the study provides strong evidence for the feasibility of CMR to detect gaps in pre-ablated scar tissue. Plus, reduction of ablation duration may translate in larger populations to detectable differences in complications, such as PV stenosis and esophageal injury.

Previous studies of LGE CMR for detection of post-ablation fibrosis were initiated by the important observation of Peters et al. (6) that the technique could successfully be applied to the left atrium (6). Several follow-up studies reported that AF recurrence was negatively associated with the extent of post-ablation fibrosis (7,8). Later, Reddy et al. (9) noted that during a case of atypical atrial flutter after PV isolation, a good entrainment site near the ostium of the right inferior PV corresponded to a gap identified by LGE CMR. Badger et al. (10) subsequently noted a fair association ($R^2 = 0.57$) between LGE regions and low voltage post-ablation. Taclas et al. (11) also reported that despite a visual and quantitative association between ablation sites on electroanatomic mapping and LGE, 20% of ablated sites revealed no LGE. In a recent study, we performed LGE CMR and high-density voltage mapping in 10 patients before repeat ablation for AF recurrence. In a generalized estimating equations model, accounting for clustering of data by individual patients, identification of scar by LGE CMR was significantly associated with reduced local bipolar voltage (-0.72 ± 0.09 mV; $p < 0.001$). However, although sites without LGE required repeat isolation for ultimate PV isolation, there was no association between LGE identified scar gaps and the earliest PV reconnection sites identified by the circular mapping catheter (12). Seventy-two percent of PV reconnection sites were seen in regions of LGE-defined scar. Our study was in agreement with the Bisbal et al. (5) study with regard to the ability of LGE CMR to identify some gaps. However, in our hands, CMR could not reliably identify the sites of earliest electrical activation into the PV. This discrepancy might be attributable to differences in magnetic field strength (1.5-T in our study vs. 3.0-T in the study by Bisbal et al. [5]), image acquisition protocol, and post-processing tools. In addition, some reconnection sites were likely smaller than the limit of resolution for CMR ($1.25 \times 1.25 \times 2.5$ mm in the study by Bisbal et al. [5]) and were therefore not visualizable, regardless of post-processing tools. Therefore, patient populations with smaller gaps due to more extensive underlying scar or differences in ablation technique might be expected to yield more disagreements between LGE and circular mapping.

Given the important implications of the findings by Bisbal et al. (5), a prospective randomized trial that would assess the utility of CMR guidance for targeting of gaps is warranted. The technology for real-time, CMR-guided procedures is rapidly advancing (13). With concurrent availability of results from studies such as that by Bisbal et al. (5), the evolution of real-time CMR guidance for electrophysiology procedures may yield the ability to detect gaps despite transient electrical stunning. Such ability, during the index procedure, would revolutionize the efficacy of AF ablation procedures.

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