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Noninvasive Imaging of Sinus Node Disease: Can It Predict the Need for Pacemaker Implantation?

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Editorial Comment

“The best way to predict the future is to invent it.” —Alan Kay, US computer scientist.

Electrophysiologic therapy for complex arrhythmias is increasingly directed at structural as well as electrophysiologic pathology. Ablation for ventricular tachycardia in patients with structural disease, while still based upon defining and locating reentrant,¹ triggered,² or automatic mechanisms,³ is increasingly targeted at myocardial scar defined invasively⁴ or noninvasively⁵ using late gadolinium enhancement magnetic resonance imaging (LGE-MRI), with substantial success.⁶ Complex macroreentrant atrial arrhythmias often involve regions of low atrial voltage whose definition can facilitate ablation.⁷ More recently, atrial fibrosis in atrial fibrillation (AF) patients, imaged using LGE-MRI has been shown in the pioneering work of the Utah group to predict postablation AF recurrence⁸ and to be inversely related to subsequent reverse remodeling.^{9,10} Their work has also shown that the degree of structural remodeling quantified by LGE-MRI may not differ between patients with and without lone AF,¹¹ suggesting its central relationship to AF rather than comorbidities, and also improves the predictive value of scoring systems for embolic phenomenon.¹² In addition, LGE-MRI imaging of the atrium can assess gaps between ablation lesions that can be targeted during repeat procedures.¹³

In this issue of the *Journal of Cardiovascular Electrophysiology*, Akoum *et al.* from the Utah group present a novel and potentially important application of imaging structural disease: The use of LGE-MRI-identified atrial fibrosis to identify sinoatrial node (SAN) dysfunction and hence the need for future pacemaker implantation.¹⁴ In this observational study of 344 AF patients, LGE-MRI before AF ablation was used to quantify atrial fibrosis on the Utah scale (Stage I, minimal fibrosis: <5% enhancement; Utah Stage II, mild fibrosis: 5–20%; Utah Stage III, moderate fibrosis: 20–35%; or Utah Stage IV, extensive fibrosis: >35%). After ablation, 22 patients (6%) required pacemaker implantation for symptomatic SAN dysfunction at 50 ± 40 days, the incidence rising with Utah stage (0, 4.5%, 10.2%, and 12.5% in Stages I–IV, respectively). On univariate analysis, Utah fibrosis stage, age, and female gender were predictors of pacemaker implantation, whereas history of persistent AF, use of antiarrhythmic drugs, beta-blockers, calcium channel blockers, and digoxin were not.

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In multivariate analysis, only Utah stage was a significant predictor of pacemaker requirement. Notably, SAN dysfunction did not reflect the extent of AF ablation—right atrial ablation was uncommon ($n = 52$; 15.2%) and, if performed, involved only the cavotricuspid isthmus. The authors concluded that atrial fibrosis detected by LGE-MRI showed preferential left atrial involvement and was associated with clinically significant SAN dysfunction.

These data are of substantial clinical interest because SAN dysfunction is one of the most common indications for permanent pacing,¹⁵ associated with AF (in the tachy-brady syndrome¹⁶) as well as structural atrial remodeling.¹⁷ Nevertheless, at the current time, SAN dysfunction is typically not predicted, but diagnosed by past symptoms such as near-syncope or syncope with evidence of sinus bradycardia or chronotropic incompetence. Sadly, surrogates such as prolonged P-wave duration¹⁸ or invasive measurements of sinus nodal function¹⁹ have been disappointing as predictors for pacing. Thus, the promise of noninvasively predicting future SAN dysfunction that requires pacemaker implantation is of great potential clinical value.

As with any good study, the work by Akoum *et al.* raises several important questions. First, the authors quantified left atrial fibrosis, which has an unclear mechanistic relationship to SAN disease. Although right atrial (RA) fibrosis was quantified in a subset of 134 patients, it did not predict SAN dysfunction on multivariate analysis. Interestingly, fibrosis in the RA was lower than in the left atrial (LA; $5.3 \pm 6.4\%$ of RA vs $16.7 \pm 11.1\%$ of LA volume), and was mostly septal with lateral RA wall involvement only in “advanced” cases. This distribution suggests that LGE-MRI fibrosis in this study may be a marker of widespread disease that also involves the SAN, rather than the mechanism for SAN dysfunction *per se*. In addition, even when fibrosis lies near the SAN, it is unclear if this affects intrinsic SAN function (attributed to membrane channels and the “calcium clock”²⁰), or its electrical coupling to atrial tissue.^{21,22} Future studies are therefore required before extrapolating these results to patients without AF and extensive atrial remodeling. Importantly, since SAN function cannot be assessed in AF, SAN dysfunction may have been underestimated in patients with recurrent AF postablation (i.e., higher Utah stage⁸). It may be valuable to link LGE-MRI with other indices of fibrosis, including prolonged electrocardiogram (ECG) P-wave duration.²³ Although one may theoretically attribute post-procedural SAN dysfunction to changes in the autonomic nervous system from AF ablation,^{24,25} elevated heart rate due to attenuation of parasympathetic innervation is typically observed.²⁶ Finally, these data raise the intriguing possibility of, and inspire future studies on, using LGE-MRI to identify fibrosis in the His-Purkinje conduction system. This would have equally important implications for guiding ventricular pacing in patients with and without AF.

How might clinicians use the results of this study? Although the rate of pacemaker implantation was low, even in the patients with most atrial fibrosis (12.5% in Utah stage IV), clinicians may be advised to follow more closely AF patients who are female, older, and with higher stages of atrial fibrosis for SAN dysfunction. Future studies should extend these analyses to AF patients not undergoing ablation, and to patients without AF.

In summary, these data show for the first time that LGE-MRI may be a valuable tool to identify patients who will require pacemaker therapy for SAN dysfunction after AF ablation. The data open the exciting possibility of using sequential LGE-MRI to assess the natural history of conducting system disease, and significantly change the way that we assess the need for pacemaker implantation. And perhaps even predict it?

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