Comparison of preexisting and ablation-induced late gadolinium enhancement on left atrial magnetic resonance imaging

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BACKGROUND Postablation atrial fibrillation recurrence is positively associated with the extent of preexisting left atrial (LA) late gadolinium enhancement (LGE) on magnetic resonance imaging (MRI), but negatively associated with the extent of postablation LGE regardless of proximity to the pulmonary vein antra. The characteristics of pre- vs postablation LA LGE may provide insight into this seeming paradox and inform future strategies for ablation.

OBJECTIVE The purpose of this study was to define the characteristics of preexisting vs ablation-induced LA LGE.

METHODS LGE-MRI was prospectively performed before and ≥3 months after initial ablation in 20 patients. The intracardiac locations of ablation points were coregistered with the corresponding sites on axial planes of postablation LGE-MRI. The image intensity ratio (IIR), defined as the LA myocardial MRI signal intensity divided by the mean LA blood pool intensity, and LA myocardial wall thickness were calculated on pre- and postablation images.

RESULTS Imaging data from 409 pairs of pre- and postablation axial LGE-MRI planes and 6961 pairs of pre- and postablation image sectors were analyzed. Ablation-induced LGE revealed a higher IIR, suggesting greater contrast uptake and denser fibrosis, than did preexisting LGE (1.25 ± 0.25 vs 1.14 ± 0.15; P < .001). In addition, ablation-induced LGE regions had thinner LA myocardium (2.10 ± 0.67 mm vs 2.37 ± 0.74 mm; P < .001).

CONCLUSION Regions with ablation-induced LGE exhibit increased contrast uptake, likely signifying higher scar density, and thinner myocardium as compared with regions with preexisting LGE. Future studies examining the association of postablation LGE intensity and nonuniformity with ablation success are warranted and may inform strategies to optimize ablation outcome.

KEYWORDS Atrial fibrillation; MRI; Late gadolinium enhancement; Fibrosis; Catheter ablation

ABBREVIATIONS AF = atrial fibrillation; CI = confidence interval; EAM = electroanatomic map; IIR = image intensity ratio; LA = left atrial; LGE = late gadolinium enhancement; MPR = multiplanar reformatted; MRI = magnetic resonance imaging; PVI = pulmonary vein isolation

Introduction

Radiofrequency catheter ablation is increasingly used for treatment of drug refractory atrial fibrillation (AF). The presence of AF is associated with left atrial (LA) scar, which is detectable by late gadolinium enhancement (LGE) cardiac magnetic resonance imaging (MRI). We recently described the image intensity ratio (IIR), calculated by normalization of the LA myocardial pixel intensity by the blood pool intensity, and validated quantitative IIR thresholds of >0.97 and >1.61 corresponding to local bipolar voltage thresholds of <0.5 and <0.1 mV, respectively. Previous studies have reported a positive association between the extent of preexisting LA LGE and AF recurrence after ablation. Paradoxically, however, the extent of postablation LGE has been described to have a negative association with AF recurrence regardless of proximity to the pulmonary vein antra. A recent study demonstrated differences in the extent and distribution of...
pre- and postablation LA LGE. We hypothesized that differences in the homogeneity of LGE vs nonenhanced myocardium, that is, the density of preexisting vs ablation-induced scar, mediate the disparate association of each LGE type with arrhythmia occurrence. In addition, regions with homogeneous scar are likely to be thinner than regions with scar and intervening surviving myocardium. Therefore, in this study we sought to examine LGE-MRI LA myocardial signal intensity and myocardial thickness differences between preexisting and ablation-induced LA LGE.

Methods

Study population
Between April 2010 and April 2013, 22 patients were prospectively enrolled to undergo cardiac MRI scans both before and at least 3 months after their initial radiofrequency catheter ablation for AF. The Johns Hopkins Institutional Review Board approved the study protocol. Written informed consent was obtained from each patient before the preprocedural MRI. Two of 22 (9.1%) patients were excluded because of insufficient imaging data, and the remaining 20 formed the study cohort.

MRI

MRI acquisition was performed using a 1.5-T MRI scanner (Avanto, Siemens, Erlangen, Germany). LGE-MRI scans were acquired within a range of 10–32 minutes (mean 17 ± 5 minutes) after 0.2 mmol/kg gadolinium injection (gadopentetate dimeglumine, Bayer Healthcare Pharmaceuticals, Montville, NJ) using a fat-saturated 3-dimensional inversion recovery–prepared fast spoiled gradient recalled echo sequence with respiratory navigation and electrocardiogram gating, an echo time of 1.52 ms, a repetition time of 3.8 ms, an in-plane resolution of 1.3 × 1.3, a slice thickness of 2.0 mm, and a flip angle of 10°. The trigger time for 3D LGE-MRI images was optimized to acquire imaging data during diastole of LA as dictated by inspection of cine images. The optimal inversion time was identified with an inversion time scout scan (median 270 ms; range 240–290 ms) to maximize nulling of the LA myocardium. A parallel imaging technique, generalized auto-calibrating partially parallel acquisition (reduction factor 2), was used. Patients with persistent AF were started on antiarrhythmic medication and referred for cardioversion 3–4 weeks before MRI and AF ablation. Of all patients, 6 were in AF at the time of baseline imaging and 5 were in AF during follow-up.

Image analysis of pre- and postablation MRI

QMass MR software (version 7.2, Leiden University Medical Center, Leiden, The Netherlands) was used to quantify LGE extent on pre- and postablation LGE-MRI by an observer that was masked to electroanatomic map (EAM) results. Epicardial and endocardial contours were manually drawn around the LA myocardium on multiplanar reformatted (MPR) axial images (3.5-mm slice thickness), which were reconstructed from axial image data (Figure 1). The anatomical reference point was set at the LA posteroseptum, and the LA myocardium in each axial plane was divided into 20 sectors. The average wall thickness of each sector was calculated. The IIR for each sector, defined as the mean pixel intensity of each sector divided by the mean pixel intensity of the entire LA blood pool, was calculated. Sectors with IIR > 0.97 and > 1.61 were labeled as LGE and dense LGE, respectively. The pulmonary vein-atrial junction and the mitral annulus were excluded from myocardial contours (Figure 1). To measure inter- and intraobserver variability, the epicardial and endocardial contouring of the entire LA was repeated for a random sample of 5 patients by a second independent observer and by the primary observer, respectively.

Electroanatomic mapping and radiofrequency catheter ablation

Radiofrequency catheter ablation using the pulmonary vein isolation (PVI) strategy was performed with an EAM system (CARTO 3, Biosense Webster Inc, Diamond Bar, CA) and a mapping/ablation catheter with a 3.5-mm open-irrigation tip (Navistar ThermoCool, Biosense Webster) in all cases. The position coordinates of all radiofrequency application sites were recorded using the EAM system. Acute PVI was achieved in all subjects. In persistent AF cases, additional ablation was performed including linear roof and floor lines. Patients were observed for 24 hours after the procedure. No immediate postoperative complications were noted.

Coregistration of electroanatomic mapping data and postablation MRI

By using previously validated custom software (Volley, Johns Hopkins University, Baltimore, MD), the coordinates of ablation points on the EAM were registered on axial planes of postablation LGE-MRI. An observer, masked...
to IIR results, performed the registration using the pulmonary venoatrial junctions, the inferior mitral valve, and the anterior base of the LA appendage as anatomical references. Image sectors that corresponded to ablation points from the EAM were defined as ablated sectors (Figure 2).

**Statistical analysis**

Continuous data are expressed as mean ± SD and categorical data as numbers or percentages. The IIR and thickness measurements from ablation-induced LGE were compared with IIR and thickness measurements from preexisting LGE by using the nonparametric Wilcoxon-Mann-Whitney test. The multivariable association of LGE type (ablation vs preexisting) as a dependent variable with IIR and thickness as independent variables was also assessed using a binary logit generalized estimating equation model, clustered by patient, and with an exchangeable correlation matrix. The intraclass correlation coefficients for interobserver variability in measuring the IIR were calculated using 2-way random effects models. Receiver operating characteristic curve analysis was performed to examine the diagnostic performance of the IIR for differentiating ablation-induced LGE from preexisting LGE. Statistical analyses were performed using STATA (version 12, StataCorp, College Station, TX).

**Results**

**Patient characteristics**

Twenty patients (10 [50%]) with paroxysmal AF and 10 (50%) with persistent AF; 16 (80%) men; mean age 59 ± 8.8 years) were enrolled in this study. Four individuals (20%) had underlying heart disease (1 [5%]) with hypertrophic cardiomyopathy, and 2 [10%] with tachycardia-induced cardiomyopathy). Left ventricular ejection fraction was 61% ± 8.6% (range 35%–75%), and CHA2DS2-VASc score was 1.2 ± 0.99 (range 0–3). The characteristics of patients are summarized in Table 1.

**Preablation MRI**

Three-dimensional LGE-MRI with minimal artifacts was obtained in all 20 patients. A total of 6961 image sectors from 409 MPR axial image planes were analyzed. Of 6961 sectors, 3000 (43%) and 57 (0.8%) sectors exhibited preexisting LGE (IIR > 0.97) and preexisting dense LGE (IIR > 1.61), respectively. The IIR and LA wall thickness of preexisting LGE were 1.14 ± 0.15 mm (range 0.97–1.99 mm) and 2.37 ± 0.74 mm (range 0.42–5.84 mm), respectively.

**Registration of EAM data to postablation MRI**

Postablation MRI was performed 287 ± 148 days after the initial AF ablation procedure. The procedural coordinates of a total of 8670 ablation points from the EAM system were registered to the postablation LGE-MRI. A total of 6691 sectors from 391 MPR postablation image planes were analyzed. A total of 1533 ablated image sectors were identified. Of 1533 ablated sectors, 1132 (74%) and 91 (5.9%) sectors exhibited ablation-induced LGE (IIR > 0.97) and ablation-induced dense LGE (IIR > 1.61), respectively. Compared with preexisting LGE sites, ablation-induced LGE sites had a significantly higher IIR (1.25 ± 0.25; range 0.97–2.75; P < .001) and thinner LA wall (2.10 ± 0.67 mm; range 0.37–4.85 mm; P < .001) (Figure 3). In the multivariable binary logit generalized estimating equation model, which was clustered by patient, the IIR (β = 2.59; P < .001) and wall thickness (β = −0.78; P < .001) were independently associated with ablation-induced LGE.

**Inter- and intraobserver variability**

A total of 1844 image sectors from 5 patients underwent repeat analysis by the same reviewer and subsequently by a second reviewer for the assessment of intra- and interobserver variability, respectively. The intraclass correlation for the intraobserver variability in IIR measures was 0.987 (95% confidence interval [CI] 0.985–0.989) for the reliability of observations. The intraclass correlation for the intraobserver variability in thickness measures was 0.929 (95% CI 0.922–0.935) for the reliability of

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**Figure 2** Registration of EAM data to postablation LGE-MRI. A: Location data of ablation sites on EAM (white square dots) were registered to the postablation MRI by using custom software. B: LA endocardial and epicardial contours are drawn onto the axial image at the same level as panel A. LA sectors on axial image planes corresponding to ablated sites were identified. In this example, sectors 7, 9, 10, and 11 were identified as ablated sectors. EAM = electroanatomic map; LA = left atrium/atrial; LGE = late gadolinium enhancement; MRI = magnetic resonance imaging; RIPV = right inferior pulmonary vein.
Table 1  Characteristics of the patients (N = 20)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>59 ± 8.8</td>
</tr>
<tr>
<td>Sex: male</td>
<td>16 (80)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>29 ± 5.6</td>
</tr>
<tr>
<td>Type of AF</td>
<td></td>
</tr>
<tr>
<td>Paroxysmal</td>
<td>10 (50)</td>
</tr>
<tr>
<td>Persistent</td>
<td>10 (50)</td>
</tr>
<tr>
<td>AF duration (y)</td>
<td>6.9 ± 5.7</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>61 ± 8.6</td>
</tr>
<tr>
<td>CHA2DS2-VASc score</td>
<td>1.2 ± 0.99</td>
</tr>
<tr>
<td>Duration from preoperative MRI to ablation (d)</td>
<td>3.3 ± 6.6</td>
</tr>
<tr>
<td>Duration from ablation to postoperative MRI (d)</td>
<td>287 ± 148</td>
</tr>
<tr>
<td>Ablation protocols</td>
<td></td>
</tr>
<tr>
<td>PVI</td>
<td>20 (100)</td>
</tr>
<tr>
<td>LA roof line ablation</td>
<td>3 (15)</td>
</tr>
<tr>
<td>CFAE ablation</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Lateral mitral isthmus linear ablation</td>
<td>0</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD or as n (%).

AF = atrial fibrillation; BMI = body mass index; CFAE = complex fractionated atrial electrogram; MRI = magnetic resonance imaging; LA = left atrial; LVEF = left ventricular ejection fraction; PVI = pulmonary vein isolation.

Discussions

To our knowledge, this is the first study to compare the characteristics of preexisting and ablation-induced LGE in the LA myocardium. The major finding of our study is that regions with ablation-induced LGE exhibit increased contrast uptake, suggesting higher scar density, and thinner myocardium as compared with regions with preexisting LGE.

Previous studies have demonstrated that the extent of preablation LGE in the LA myocardium positively associates with AF recurrence after catheter ablation.8,11,12 In contrast, the extent of postablation LGE in the LA myocardium negatively associates with AF recurrence regardless of the LGE proximity to the pulmonary vein antra.14–16 Studies from our group as well as others have shown that LGE, with its current resolution, is incapable of detecting all ostial PVI lesions and gaps.19–21 Therefore, it is unlikely that the presence or absence of gaps mediates the disparate association of the extent of preexisting vs ablation-induced LGE with the outcome of AF ablation. The characteristics of preexisting vs ablation-induced LGE as a possible mediator of the paradoxical association of each LGE type with outcome have not been previously investigated.

Previous experimental animal studies have demonstrated that by 2 months after radiofrequency ablation, the myocardium undergoes contraction necrosis and exhibits fibrous scar.22 LGE-MRI is able to depict not only ventricular but also atrial ablation sites as LGE regions.9,16,23 In our study, the normalized signal intensity of ablation-induced LGE was significantly higher than that of preexisting LGE. This finding indicates that ablation-induced LGE exhibits different contrast kinetics with greater uptake and/or slower washout of contrast, suggesting more severe fibrosis. A thinner wall was also noted in regions with ablation-induced LGE, which is consistent with previous histological reports of contraction necrosis at ablated sites.22 Although this study demonstrated statistically significant differences in the IIR and LA wall thickness between preexisting LGE and ablation-induced LGE, there was a significant overlap between the ranges of these measures for each LGE type (Figure 3). Nevertheless, important associations of LGE intensity and myocardial thickness with ablation were demonstrated in this study. These results indicate that scar density and nonuniformity may explain the disparate association of pre- and postablation LGE with AF recurrence in previous studies. Future studies examining the association of postablation LGE intensity and nonuniformity with AF recurrence are warranted and may inform strategies to optimize ablation outcome.

Figure 3  Distribution of the IIR and wall thickness in preexisting and ablation-induced LGE. The violin plots (light blue) show the probability density of the IIR (A) and wall thickness (B) for all LA myocardial sectors with preexisting and ablation-induced LGE. The white dot shows the median value, and the dark blue box represents the interquartile range, with the dark blue vertical line extending to the lower and upper adjacent values. IIR = image intensity ratio; LA = left atrial; LGE = late gadolinium enhancement.
Study limitations
The patient sample size is relatively small. However, many distinct nonablated and ablated image sectors per patient were analyzed. Therefore, statistical power was sufficient for testing the study hypothesis. Our results may be limited by a possibility of positional errors when registering EAM ablation points to corresponding sectors on LGE-MRI on the basis of the registration information obtained by using the EAM software. The LGE-MRI sequence used in this study provided a (1.3 × 1.3)-mm in-plane resolution and was obtained during ventricular diastole/atrial systole, thus minimizing potential negative effects of motion blurring on atrial wall thickness measurements. Nevertheless, atrial wall thickness may be near the limit of image resolution in some cases. Because of volume averaging, the analyzed LA wall sector may have included blood pool or epicardial fat in some cases. Of all MRI examinations, 27% were performed during AF; however, we found no evidence of association between rhythm at the time of imaging and the IIR (β = 0.04; P = .211). Information regarding the duration of radiofrequency application and contact force at each site was unavailable. Therefore, ablated sectors in the present study may have included sectors with ineffective lesion delivery.

Conclusion
Our study demonstrates that LA ablation–induced LGE is associated with greater contrast affinity and thinner walls as compared with preexisting LA LGE. These findings support the presence of dense fibrosis in ablated regions and may underlie the paradoxical association of each LGE type with arrhythmia recurrence.

References