Tailored Management of Atrial Fibrillation Using a LGE-MRI Based Model: From the Clinic to the Electrophysiology Laboratory

GASTON R. VERGARA, M.D. and NASSIR F. MARROUCHE, M.D.

From the Comprehensive Arrhythmia Research and Management (CARMA), University of Utah, Salt Lake City, Utah, USA

Tailored Management of Atrial Fibrillation with LGE-MRI. Ablation provides a good therapeutic alternative for atrial fibrillation (AF) management; however, its effectiveness relies in adequate patient selection. Late gadolinium enhancement-magnetic resonance imaging (LGE-MRI) allows for atrial arrhythmic substrate, as well as postablation scarring visualization. In this article, we describe a new staging system for AF based on the amount of left atrial enhancement on LGE-MRI (Utah I ≤ 5%, Utah II > 5–20%, Utah III > 20–35%, and Utah IV > 35%). On the basis of patient stage, a more tailored approach to AF management can be taken. This includes triaging appropriate candidates for ablation (Utah stages I–III), as well as anticoagulation management based on an increase on the predictive statistics of the CHADS2. LGE-MRI also allows for ablation lesion characterization. Acute edema, defined as enhancement on T2-weighted MRI images immediately post-AF ablation correlates with low voltage areas but not with LGE-MRI-defined scar. Post-AF ablation LGE-MRI scans show significant heterogeneity in the atrial wall on portions subject to radiofrequency (RF). We have postulated that some of these areas correspond to no-reflow type phenomenon. Postablation LGE-MRI can also help identify breaks in lesion sets and its correlation with conduction recovery has been used successfully to guide redo procedures. Real-time MRI-based ablation system has the potential advantage of tissue lesion visualization during RF delivery. To that end, we have developed a 3-Tesla-based real-time MRI ablation system. We demonstrated the feasibility to safely navigate, pace, and record intracardiac EGMs in the atrial chambers, as well as applying RF energy while directly visualizing lesion formation in real time. (J Cardiovasc Electrophysiol, Vol. pp. 1-7)

Introduction

Atrial fibrillation (AF) is associated with atrial electrical, contractile, and structural remodeling. Several different structural markers have been proposed and associated with ablation outcomes. However, modalities allowing providers to accurately and prospectively assess atrial structural arrhythmic substrate and to individually predict treatment outcomes are still lacking.

Although AF ablation seems to be a valid therapeutic option, the effectiveness of the procedure has been demonstrated only in a moderate percentage of the AF patient population. Thus, the dilemma lies in defining the appropriate ablation candidate that would profit most from an invasive procedure. Furthermore, success of the radiofrequency (RF) ablation procedure correlates with the appropriateness of transmural left atrial lesion. However, accurate intraprocedural assessment of lesion formation remains yet to be determined.

Gadolinium is a magnetic resonance imaging (MRI) contrast agent, which allows differentiation between healthy and abnormal myocardial tissue due to differential washout kinetics. These properties have led to the development of late gadolinium enhancement (LGE)-MRI. By using custom-made high-resolution LGE-MRI sequences, we have been able to define areas of enhancement within the atrial wall, which correspond to intramyocardial fibrosis and/or ablation scar.

In this article, we describe an MRI-based tailored approach to manage patients with AF. Our protocol begins with clinical staging of AF capable of predicting ablation success and patient’s stroke risk. Finally, we demonstrate the use of MRI in planning redo AF ablation procedures, and an overview of our work in the field of real-time MRI.

Personalized Approach to AF Management

On initial clinical evaluation and after determining the AF burden, we acquire a cardiac MRI to develop a personalized management approach. Cardiac MRI allows assessment of left atrial wall structure including the amount of fibrosis within the myocardial tissue allowing us to stage the structural progression of AF.
Figure 1. LGE-MRI quantification of pre-ablation fibrosis/structural remodeling and postablation scarring. After LGE-MRI images are obtained (Step 1), the endocardial and epicardial borders are manually contoured and isolated (Steps 2 and 3), and the extent of LGE is then quantified using the pixel intensity distribution (Step 4). Qualitative confirmation is then performed, a color lookup table mask is then applied to better differentiate enhanced and nonenhanced tissue (Step 5), and finally a 3-dimensional rendering of the left atrium is generated allowing for better visualization and spatial localization of the late gadolinium enhancement (Step 6).

MRI Image Acquisition

All studies are obtained either on a 1.5 Tesla Avanto or on a 3.0 Tesla Veerio scanners (Siemens Medical Solutions, Erlangen, Germany) using a TIM phased-array receiver coil (Siemens Medical). The scan is acquired 15 minutes after 0.1 mmol/kg Multihance (Bracco Diagnostic Inc., Princeton, NJ, USA) contrast agent injection, using a 3-dimensional inversion recovery, respiration-navigated, electrocardiogram (ECG)-gated, gradient echo pulse sequence. Typical acquisition parameters are free breathing using navigator gating, a transverse imaging volume with voxel size $= 1.25 \times 1.25 \times 2.5$ mm (reconstructed to $0.625 \times 0.625 \times 1.25$ mm), TR/TE = 5.4/2.3 ms, flip angle $= 20^\circ$, inversion time (TI) = 270–310 ms, and generalized autocalibrating partially parallel acquisition (GRAPPA) with R = 2 and 46 reference lines. ECG gating is used to acquire a small subset of phase-encoding views during the diastolic phase of the left atrium (LA) cardiac cycle. The time interval between the R peak of the ECG and the start of data acquisition is defined using the cine images of the LA. Fat saturation is used to suppress fat signal. The TE of the scan (2.3 ms) is chosen such that fat and water are out of phase and the signal intensity of partial volume fat-tissue voxels is reduced allowing improved delineation of the LA wall boundary. The TI value for the LGE-MRI scan is identified using a scout scan. Typical scan time for the LGE-MRI study is 5–10 minutes, depending on subject respiratory and heart rates.

LGE-MRI Quantification of Pre-Ablation Fibrosis/Structural Remodeling and Postablation Scarring

After image acquisition, the epicardial and endocardial LA borders are manually contoured using the CoreView image display and analysis software (MARREK Inc., Salt Lake City, UT, USA). The relative extent of pre-ablation enhancement and postablation scar are then quantified within the LA wall with a threshold-based algorithm utilizing pixel intensities from normal based on a bimodal distribution (Fig. 1).

Staging AF Using MRI

On the basis of prospective outcome data from a 330 patient series that have undergone pre-AF ablation LGE-MRI, we have established a clinical staging system composed
of 4 stages based on the amount of pre-ablation delayed enhancement (fibrosis) as a percentage of the volume of the left atrial wall. This clinical staging system includes 4 stages that are Utah I ≤ 5% enhancement, Utah II > 5–20%, Utah III > 20–35%, and Utah IV > 35% (Fig. 2).

When performing a multivariate Cox regression analysis that included age, left atrial volume, postablation number of PV encircled, and total scar, we found that number of PV isolated in patients with Utah stage II and that the total amount of scar in those with Utah stage III are predictors of success. Those patients with minimal pre-ablation fibrosis, Utah stage I, did well, regardless of the number of pulmonary vein (PV) isolated or the total amount of scar, whereas those with advanced atrial remodeling as assessed by LGE-MRI, Utah stage IV, did poorly. When performing a multivariate Cox regression analysis that included age, left atrial volume, postablation number of PV encircled, and total scar, we found that number of PV isolated in patients with Utah stage II and that the total amount of scar in those with Utah stage III are predictors of success. Those patients with minimal pre-ablation fibrosis, Utah stage I, did well, regardless of the number of pulmonary vein (PV) isolated or the total amount of scar, whereas those with advanced atrial remodeling as assessed by LGE-MRI, Utah stage IV, did poorly. Moreover, in a multivariate regression model, LGE-MRI evaluation of the left atrial substrate was shown to improve the predictive value of the CHADS2 score, allowing us to define patients at higher risk of stroke despite having a low or moderate CHADS2 score.

A total of 387 patients were included for analysis in this study; of these, 36 (9.3%) had a history of stroke. Those patients with a previous stroke had a significantly higher percentage of LA fibrosis compared with those without (24.4% ± 12.4% versus 16.1% ± 9.8%, P ≤ 0.001). There was a significant difference in the rate of thromboembolism between patients with stage I and those with stage IV of atrial remodeling as assessed by LGE-MRI. Patients with higher risk for stroke (CHADS2 score ≥ 2) had higher amounts of LA fibrosis. Using uni- and multivariate regression analysis, LGE-MRI quantified left atrial structural remodeling was independently associated with stroke.

When calculating the clinical predictors for stroke, excluding stroke itself (CHADS2 Score), the predictive statistics of this model increased after adding MRI-based LA structural remodeling. On the basis of this staging system, we have developed a comprehensive MRI-based AF management algorithm (Fig. 3), which helps us in triaging patients to AF ablation, as well as planning a corresponding ablation strategy and future anticoagulation strategy.

To further study and substantiate these findings, a randomized trial is currently under way. We are currently enrolling patients for a large prospective observational study: the Delayed-Enhancement MRI Determinant of Successful Radiofrequency Catheter Ablation of Atrial Fibrillation (DEECAF), in which we will attempt to apply our findings in a multicenter, prospective trial.

**RF Ablation Lesion Characterization**

All of our patients who do not have a contraindication undergo an immediate postablation cardiac MRI at 3, 6, 12, 24 months and every other year, thereafter to allow us to differentiate between the location and amount of edema versus transmural lesions initiated during the ablation procedure.

**Acute Atrial Wall Edema Post-AF Ablation**

Acute edema, enhancement on T2-weighted (T2w) images performed immediately after AF ablation, correlated significantly with low voltage areas (defined as <0.05 mV) mapped using the CARTO system. However, the area enhanced with T2w imaging is much larger than the area covered by LGE on MRI acutely post-AF ablation (Fig. 4) (unpublished data). Immediately, postablation edema is seen not only in regions directly subjected to RF energy but also in distant regions, and it does not predict final scar formation (Fig. 5) defined by LGE-MRI at 3 months. An MRI 3 months after ablation shows loss of enhancement on T2w images, consistent with edema resolution in areas free of scar. Edema seen acutely in regions other than in ablated areas suggests a mechanism other than direct RF thermal lesion as its cause.
Finally, the presence of edema in regions away from areas that result in scar formation as well as its association with low voltage on electroanatomical mapping may explain, at least partially, the presence of acute PV disconnection and late reconnection with edema resolution.

**Late Gadolinium-Enhanced Defined Scar and Nonreflow Phenomenon**

Significant heterogeneity in the LA wall is seen on acute postablation LGE-MRI scans with portions showing very little or no enhancement at all, even in areas that received direct RF energy (Fig. 5). In a porcine model of ablation, they correlate well to lesion formation, particularly to areas with the highest amount of injury (Fig. 6). We believe that these areas of no enhancement correspond to areas of nonreflow, phenomenon similar to that seen in ventricles.

**Late Imaging and Recurrences**

The amount of scar and the number of circumferentially scarred pulmonary vein antrum (PVA) on LGE-MRI is associated with better outcomes and confirm earlier studies that total LA ablation scar burden is associated with AF termination. However, complete PVA isolation as defined by LGE-MRI is difficult to achieve and is complicated by the fact that certain changes seen acutely are reversible over a 3-month period.

In the acute postablation period, voltage-defined scar and LGE-MRI-defined scar do not have a good correlation (Fig. 5). Acute LGE-MRI areas correlate well with areas of low voltage at 3 months. These areas of acute LGE-MRI likely represent areas with irreversible damage from RF ablation, whereas the larger area of low voltage during the acute postablation period likely represents a combination of tissue edema, other reversible changes, and areas that will scar completely.

LGE-MRI can accurately identify the location of breaks in ablation lesion sets, and its correlation with conduction recovery, which may explain postablation AF recurrences. Our study demonstrated that AF recurrences following ablation are associated with significant gaps between lesions, and that these gaps correlated well with recovery of local electrograms (EGMs) or PV electrical conduction. This allows us to better plan and tailor redo procedures for patients with PV tachycardias, atrial/flutters, or AF. For example, a patient who would have...
Figure 5. Postablation edema and scar distribution, temporal extension, and resolution. At baseline no edema, enhancement on T2w images, is seen (1). Immediately postablation, edema is seen not only on regions directly subjected to RF energy but also in distant regions (2). At 3 months, there is resolution of acute edema, as evidenced by resolution of T2w enhancement, with persistence of scar (3). An image of immediately postablation edema (4) is superimposed to, and more extensive than, the scar as defined by LGE-MRI (5). By masking the areas with late gadolinium enhancement and superimposing them over those with T2w enhancement, this relation becomes more evident (6). This illustrates the more widespread nature of LA wall edema post-AF ablation when compared with final scar.

Figure 6. LGE-MRI acute heterogeneity and nonreflow phenomenon. Immediate postablation LGE heterogeneity. Areas with clear enhancement mixed with areas with no enhancement at all (blue arrows in panels 1 and 2) in the atrial wall in areas heavily exposed to RF energy. These areas of nonenhancement on acute scans predict scar formation well at 3 months (blue arrows in panels 3 and 4).
usually not been considered for early repeat ablation due to early recurrence of sustained atrial arrhythmia 3 weeks after his first AF ablation procedure was taken to the laboratory for mapping and ablation of atrial tachycardia (AT). The decision was triggered by a repeat MRI revealing a large gap in scar formation along the roof of the right superior PV antrum, an area that correlated with surface P-wave morphology. As demonstrated in Figure 7, selective ablation in this region resulted in isolation of the PV and termination of the tachycardia.

The Road to Real-Time MRI

Real-time MRI-based imaging and ablation system has the potential advantage of atrial tissue lesion visualization during RF delivery, which could be used as an ablation end point. At our EP-MRI suite, we could demonstrate the feasibility to safely navigate and pace, and record intracardiac EGMs in the atrial chambers under 3-Tesla real-time MRI guidance. We have also been able to create lesions applying RF energy delivered while imaging the atrial tissue in real time (with a T2w half-Fourier acquisition single-shot turbo spin-echo [HASTE] MRI sequence) and as the lesions were being created. Furthermore, we could accurately correlate the presence of enhancement on these T2w HASTE images of lesion formation with well-defined postablation and ex vivo LGE-MRI images, demonstrating tissue damage and the presence of lesions on ex vivo gross examination of the heart [submitted for publication]. Real-time MRI-guided ablation has the potential to be the primary ablation option for all patients with AF.

MRI Limitations and Challenges

We recognize that the inherent limitations to the adoption of an MRI-based approach in the daily practice of a busy electrophysiologist still exist. A significant challenge for inexperienced MRI laboratories is scanning optimization for good quality atrial image acquisition. Despite this fact, in the past 3 years, major progress has been described at ours and also other institutions reporting improvements in the quality of MRI scan acquisition and hence usability of the atrial MRI scans in AF and other arrhythmia patients.

Another major limitation is the accessibility to an electrophysiology magnetic resonance imaging (EP-MRI) or cardiac MRI scanner at various institutions. Nevertheless, MRI scanner manufacturers have recognized the EP-MRI-based concept to be an essential diagnostic and therapeutic product that can help arrhythmia patients. This fact would be extremely helpful in promoting the installation and adoption of MRI scanners in a significant number of cardiology practices and EP laboratories in the years ahead.

References


4. Segerson NM, Daccarett M, Badger TJ, Shabaan A, Akoum N, Fish EN, Rao S, Burgon NS, Adjei-Poku Y, Kholmovski E, Vijayakumar S, DiBella EV, MacLeod RS, Marrouche NF: Magnetic
