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Role of Magnetic Resonance Imaging in Atrial Fibrillation Ablation

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Introduction

Atrial fibrillation (AF) is the most common arrhythmia, with a prevalence of 1.0–1.5% in the general population and up to 10% in the elderly [1]. AF results from and also leads to structural and electrical atrial remodeling. Catheter ablation has recently emerged as a viable option to reduce AF symptoms and to avoid consequences associated with long-term pharmacological therapy. However, the efficacy of ablation for AF is suboptimal, particularly in patients with persistent or longstanding persistent AF. Additionally, there are no clear survival benefits for patients undergoing the procedure compared to those treated conservatively [2]. Procedural outcomes must be optimized, especially given the fact that complications related to AF ablation are not negligible.

Cardiovascular magnetic resonance (CMR) has become the gold standard for non-invasive myocardial tissue characterization [3]. Additionally, CMR is frequently used to define cardiovascular anatomic and functional variations across patients. The absence of ionizing radiation adds to the utility of CMR as a tool for longitudinal assessment of the arrhythmic substrate with serial examinations. Therefore, CMR can be used to inform patient selection for ablation, assess thromboembolic risk, and provide arrhythmic substrate information before, during, and after catheter ablation. Here, we will review the role of CMR prior to, during, and after AF ablation.

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Compliance with Ethics Guidelines

Conflict of Interest

Dr. Roy Beinart declares no potential conflicts of interest.

Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

Pre-ablation CMR

CMR for the assessment of left atrial geometry and function

AF evolves from a set of complex events that typically initiate with triggers originating from the pulmonary veins. At AF onset, the atrium can exhibit normal structure and conduction characteristics. However, over time, electrical and structural changes that occur favor AF sustenance [4-6]. In fact, AF appears to promote changes in atrial electrophysiology properties that promote its perpetuation. An essential property of the electrical remodeling that favors AF sustenance is the decrease in atrial refractoriness [7]. Importantly, the decrease in atrial refractoriness is spatially heterogeneous [8]. Additional atrial remodeling features include increased expression of intercellular gap junctions and conduction velocity shortening [9-11], in addition to sinus node dysfunction [12].

In parallel to electrical remodeling, atrial structural remodeling also occurs, which consists of increased atrial myocyte apoptosis and resultant fibrosis, as well as compensatory hypertrophy and dilation. Atrial fibrosis, which is reportedly facilitated via the TGF- β pathway, is extremely important in the creation of arrhythmogenic substrate and support of re-entry circuits. Interestingly, the left atrial free wall near the pulmonary vein antra exhibits significant fibrosis [13-15].

From an anatomical standpoint, CMR is capable of providing detailed images and analyses regarding LA geometry and surrounding structures [16]. An excellent correlation has been demonstrated between atrial volumes measured by CMR and actual volumes assessed in cadaveric casts [17]. Prior CMR studies have also revealed that patients with AF have larger LA volumes compared to healthy participants [18, 19]. In contrast, patients with “lone AF” appear to have similar atrial volumes to healthy volunteers [20]. Moreover, CMR studies have demonstrated that LA volume is larger in patients with persistent versus paroxysmal AF [21]. It should be noted that CMR image acquisition during AF can be challenging and may necessitate repeat acquisitions and adjustments to the triggering window. Nevertheless, measuring both atrial and ventricular volumes during AF is feasible, and accurate measurements can be achieved using real-time cine sequences [22].

Atrial function can be accurately assessed by CMR. Therkelsen and colleagues demonstrated improvements in atrial contractile function in patients with persistent AF beginning 24 hours after cardioversion, with continuing improvement through 180 days. Interestingly, while right atrial volumes were completely normalized at 180 days post-cardioversion, the left atrial and ventricular function did not completely recover in that time period [23].

Importantly, CMR can accurately define pulmonary vein (PV) anatomy, anomalies, and branching patterns. Accurate anatomic images are essential for correct identification of the PV ostia as a target for linear ablation lesions. To improve the localization of ostia and to optimize consistency, PV dimensions are measured in the sagittal plane at which the PVs separate from each other and the LA [24]. Similar to the LA, PV dimensions change over time during AF [18]. However, the change in PV dimensions does not correlate with the origin of arrhythmogenic trigger foci [25].

CMR for the assessment of left atrial myocardial characteristics

One of the unique features of CMR is the ability to characterize myocardial tissue composition even for thin-walled tissues such as the LA wall. The feasibility of atrial late gadolinium enhancement magnetic resonance imaging (LGE-CMR) was initially reported by Peters and colleagues, who found no evidence of LGE in 23 AF patients who underwent CMR prior to ablation. Post-ablation, however, LGE was detected in all patients [26]. In contrast, Oakes and colleagues reported the utility of LGE-CMR for visualization of pre-existing left atrial myocardial prior to the ablation procedure. The authors categorized patients based on the extent of myocardial enhancement, which showed that the extent of fibrosis was associated with AF type (paroxysmal versus persistent) prior to ablation and with AF recurrence post-ablation. In addition, they noted a strong association between regions of enhancement and low voltage on electroanatomic maps [27]. Subsequently, Mahnkopf and colleagues reported a pre-ablation LGE prevalence of 14.1% and 16.9% in patients with lone AF and those with comorbidities, respectively. In this and subsequent papers from the Utah group, the extent of pre-existing scar has been categorized by Utah score as follows: Group I: <5%, Group II: 5-20%, Group III: 20-35%, and Group IV: >35% atrial LGE. In the Mahnkopf and colleagues study, the distribution of pre-ablation atrial LGE was not related to AF type [28].

The estimation of scar based on image intensity, which is measured in arbitrary units, limits the objectivity of thresholds for scar detection and inter-patient comparisons of scar extent. Although LA wall image intensity on LGE-MRI varies primarily as a function of gadolinium retention in fibrotic regions, it is also affected by parameters such as surface coil proximity, contrast dose, delay in time of image acquisition after contrast injection, patient hematocrit, glomerular filtration rate, and body mass index (BMI). Our group has recently developed and validated a normalized measure, the image intensity ratio (IIR), for assessment of scar. This measurement was found to be closely associated with intracardiac voltage as a surrogate of atrial fibrosis. We believe that IIR utilization will improve the validity and reproducibility of inter-patient as well as longitudinal intra-patient comparisons of scar extent [29].

In addition, we recently studied the feasibility of measurement and range of T1 relaxation times for quantification of diffuse LA fibrosis in patients with AF. It had previously been shown that an inverse linear relationship existed between contrast-enhanced left ventricular myocardial T1 time and the burden of global myocardial fibrosis. We applied this technique for the first time to the assessment of myocardial characteristics in the left atrium, in which we found shorter median LA T1 relaxation times in AF patients compared to healthy volunteers, suggesting increased diffuse fibrosis in AF patients. Furthermore, AF patients with prior ablation had shorter T1 relaxation times compared to patients without prior ablation. We further established an association between LA T1 relaxation times and intracardiac bipolar LA voltages [30]. There is increasing evidence from our group as well as others that LGE-CMR is capable of accurate detection and quantification of LA fibrosis prior to the ablation procedure, and may have the potential for use in selecting appropriate candidates with higher odds of post-procedural AF suppression.

CMR and stroke risk in AF patients

Stroke is one of the most devastating complications of AF. Most stroke events that occur in patients with non-valvular AF are thought to arise from clot formation in the left atrial appendage (LAA) [31, 32]. Therefore, imaging of the LAA has been established as an additional risk stratification tool for identification of candidates for anticoagulation or appendage exclusion. While transesophageal echocardiography (TEE) is an acceptable clinical tool to identify clots in the LAA, it requires esophageal intubation and carries a small but significant risk for serious complications. Several studies have suggested a role for two- and three-dimensional transthoracic echocardiography (TTE) with similar discrimination indices as two-dimensional TEE for identification of LAA thrombus. A suboptimal acoustic window in some patients [33, 34], however, is a limiting factor.

CMR is a non-invasive tool that enables accurate assessment of the LAA structure and contents. Ohyama and colleagues assessed the utility of unenhanced CMR to detect clots in the LAA of 50 patients with non-valvular AF and previous CVA, and reported that MRI could easily visualize LAA thrombus in such patients. When compared to TEE, CMR had similar accuracy in characterizing LAA dimensions. Thrombus sizes were 20% larger when assessed by unenhanced CMR, however, leading the authors to suggest that CMR may be more sensitive for thrombus detection [35]. Mohrs and colleagues later performed a similar assessment, comparing TEE to contrast-enhanced CMR in 25 patients. Unlike the previous study, Mohrs reported a lack of diagnostic accuracy in detecting LAA thrombus when compared with TEE. CMR yielded sensitivity and specificity of only 47% and 50%, respectively, and positive and negative predictive values of 73% and 25%, respectively. These conflicting results may be due to either the inaccuracies of TEE as a gold standard or insufficient spatial resolution in the contrast-enhanced CMR protocol utilized in the study [36]. Additional large multicenter studies are needed before the routine use of CMR can be adopted for detection of LAA thrombus.

Several risk stratification schemes, including the CHADS2 score and CHA2DS2-VASc scores, are currently used for patient risk stratification and determining candidacy for anticoagulation [37-39]. These schemes are imperfect in predicting thromboembolism, however, and individualized factors regarding LA and LAA morphology may improve their discriminative power. Beinart et al., for example, showed an association between stroke risk and larger LAA dimensions [40]. We and others have also shown that certain LAA characteristics such as extensive trabeculations, as assessed by CMR, are associated with increased CVA risk [41, 42]. Fyrenius and colleagues assessed LA blood flow patterns in healthy volunteers and observed vortical flow during systole and diastolic diastasis that may prevent left atrial stasis and clot formation during sinus rhythm [43]. LA blood flow characteristics during AF and associated role in thrombus formation are areas that warrant further study. Additionally, Daccarett and colleagues reported a strong positive association between LA LGE and prevalent stroke, which remained significant after adjustment for clinical stroke risk variables [44]. As such, LA myocardial scar quantification and LAA morphologic assessment by CMR may optimize patient selection for anticoagulation.

CMR for intra-procedural guidance of AF catheter ablation

Haïssaguerre and colleagues first reported that local radiofrequency catheter ablation of ectopic PV triggers could suppress AF [45]. AF ablation techniques and technologies have rapidly evolved since the inception of the idea to target PV triggers [46]. The success rate of this procedure, however, remains modest, with a rate as low as 57% for a single procedure and 71% with multiple procedures [2]. Better patient selection enabled by CMR may help to improve these success rates. Additionally, pre-procedural CMR is currently used as a non-invasive imaging tool to define LA geometry and the best procedural strategies for PV isolation. The integration of pre-procedural 3D imaging with electroanatomic map data has been shown to improve procedural success and safety [47]. Bertaglia and colleagues reported their experience using MRI in patients with paroxysmal AF that underwent circumferential pulmonary vein isolation (PVI), indicating that the use of image integration significantly improved clinical outcomes [48]. In contrast, Caponi and colleagues, who compared the use of image integration versus electroanatomic mapping alone, reported that clinical outcomes were similar between the groups. In their study, the main advantage of using CMR image integration was reduced fluoroscopy time and radiation exposure [49].

CMR can also provide information regarding targets for AF ablation. In addition to LA volume as an independent predictor for AF recurrence post-ablation [50, 51], PV anatomical characteristics also correlate with ablation success and may provide important data regarding ablation strategies [52]. Oakes and colleagues found that the extent of LA fibrosis was the most significant predictor for AF ablation outcome. Moreover, higher success rates were documented when late enhancement was limited to the interatrial septum and posterior LA wall [27]. As such, the targeting of pre-existing fibrosis in certain areas of the LA will likely play a role in formulating future ablation strategies. Finally, Wong and colleagues reported an association between the extent of pericardial fat and AF severity [53]. It is well known that pericardial fat pads contain autonomic ganglia and therefore may serve as important targets for AF suppression.

Taken together, the above studies suggest that real-time CMR guidance may a) provide better visualization of the LA geometry, PV position, and anatomic features, b) reduce radiation exposure, c) improve the rapid recognition of complications such as pericardial effusion or collateral damage to adjacent structures such as the esophagus, d) provide real-time information about targets for ablation such as regions with heterogeneous fibrosis or adjacent fat pads, and e) provide real-time feedback regarding the completeness of linear ablation sets. While we and others have made significant advances toward integration of real-time CMR guidance for ablation procedures [54], many technical challenges remain before real-time CMR guidance can be fully integrated into standard EP laboratories.

CMR for assessment of lesion integrity after AF ablation

CMR has been used post the ablation procedure to assess changes in scar burden and visualize lesion formation. In addition, CMR can be used to evaluate the effects of ablation on LA geometry and function and to identify PV stenosis. Peters and colleagues performed CMR examinations on 35 patients within 3 months after AF ablation, noting that AF recurrence was negatively associated with LA scar formation [55]. Similarly, McGann and

colleagues reported that arrhythmia recurrence was negatively associated with LA scar formation at 3 months post-ablation [56]. The same authors later performed a 3-Tesla CMR study of 37 patients that underwent scans before, immediately after, and 3 months post-AF ablation. In this study, RF ablation resulted in heterogeneous lesion formation, including hyper-enhanced lesions and non-enhanced cores. The non-enhancing segments, which signify areas with micro-vascular obstruction, were associated with scar at 3 months post-ablation. In addition, the degree of scar formation at 3 months post-ablation was associated with ablation outcome at 1 year [57]. Segerson and colleagues examined the association of scar formation in an LGE-CMR study, with clinical success. The authors found that an increase in posterior and septal scar as assessed by CMR was associated with lower AF recurrence rates [58].

Hof and colleagues performed CMR 4 months after PV isolation and reported decreased LA size irrespective of AF recurrence, which suggests that the decreased LA size is a result of ablation rather than reverse remodeling [59]. Similarly, utilizing CMR, Nori and colleagues examined the effect of ablation on global and regional LA wall motion and found that there was a significant decrease in LA volume by 3 months post-ablation. In addition, prior to ablation, patients with paroxysmal AF had similar global and regional LA function to healthy volunteers. Post-ablation, however, measurements revealed decreases in several indices, including LA transport function and regional function in the LA lateral wall. In contrast, patients with persistent AF benefited from post-ablation improvements in both global and regional LA function. The authors concluded that positive reverse remodeling secondary to restoration of sinus rhythm may outweigh the negative effects of ablation [19]. Wylie Jr. and colleagues likewise demonstrated decreased LA volumes after the ablation procedure. However, they reported that while LA ejection fraction decreased in the majority of patients, RA ejection fraction increased. The authors also reported a linear association between LA scar burden and change in LA ejection fraction ($r=0.75$, $p<0.001$) [60]. Tsao and colleagues evaluated the change in PV and LA size a year after ablation, reporting a borderline decrease in LA volume in patients without AF recurrence but an increase in those with AF recurrence. In addition, the authors observed a reduction of the ostial area of the superior PVs and a rounder shape of the ostia after successful ablation. Interestingly, in patients with AF recurrence, there was further PV enlargement [61].

AF ablation can also result in symptomatic PV stenosis, a complication that appears to be under-recognized [62]. CMR can aid in detecting PV stenosis and is comparable in diagnostic indices to invasive angiography. Dill and colleagues validated the use of CMR as a tool for assessment of PV dimensions in 46 patients that also underwent angiography after AF ablation. The authors noted a significant diameter reduction in 18% of the treated PVs [63]. Similarly, Arentz and colleagues evaluated the risk for significant PV stenosis in 47 patients that underwent AF ablation, with follow-up examinations at 2 years. The authors reported that 28% of patients exhibited PV stenosis, and that distal ablations inside the PV were associated with the highest risk of stenosis [64]. More recently, Dong and colleagues reported PV stenosis in 38% of treated PVs, while significant stenosis occurred in only 3.8% of PVs [65].

Conclusions

The capability for non-invasive characterization of the LA myocardium and PV anatomy is an important adjunct for AF ablation patient selection, procedural planning, and post-procedural evaluation. CMR enables detailed assessments of LA functional and structural characteristics without exposing the patient to radiation. High costs and the expertise required for appropriate image acquisition and analysis limit the routine use of CMR. Additional advances to enhance image resolution and analysis may improve the generalizability of this technique to daily practice.

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* Of importance

** Of outstanding importance

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Association (AHA); Asia Pacific Heart Rhythm Society (APHRS); Society of Thoracic Surgeons (STS); Endorsed by the governing bodies of the; American College of Cardiology Foundation; American Heart Association; European Cardiac Arrhythmia Society; European Heart Rhythm Association; Society of Thoracic Surgeons; Asia Pacific Heart Rhythm Society; Heart Rhythm Society. 2012 HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design: a report of the Heart Rhythm Society (HRS) Task Force on Catheter and Surgical Ablation of Atrial Fibrillation. *Heart Rhythm* : the official journal of the Heart Rhythm Society. 2012; 9:632–696. Developed in partnership with the. a registered branch of the. [PubMed: 22386883]

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Opinion Statement

Ablation therapy is widely used for treatment of drug-resistant atrial fibrillation (AF). Ablation success for AF, however, is relatively low, often requiring repeated procedures for long-term suppression of the arrhythmia. Utilization of imaging techniques that visualize cardiac anatomy, function, and tissue characteristics may improve ablation results. Compared to other imaging modalities, cardiac magnetic resonance (CMR) has several advantages, including the lack of ionizing radiation and unsurpassed soft tissue resolution. Chamber morphology images can be registered onto electroanatomic maps acquired during the procedure, thus improving procedural safety and efficacy. In addition, the ability of CMR to characterize myocardial tissues may optimize patient selection for ablation and thromboembolic risk stratification. Post-procedure CMR can be used to detect potential complications, and with improved resolution, it has the potential to assess the integrity of ablation lesions. In this paper we will review the role of CMR in the pre-ablation diagnostic workup of AF patients as well as during and after catheter ablation.