Published in final edited form as:

Pacing Clin Electrophysiol. 2020 February ; 43(2): 159–166. doi:10.1111/pace.13853.

Left Ventricular Extracellular Volume Expansion does not Predict Recurrence of Atrial Fibrillation following Catheter Ablation

Suvai Gunasekaran, MS^{1,2}, Daniel C. Lee, MD³, Bradley P. Knight, MD³, Jeremy D. Collins, MD^{1,4}, Lexiaozi Fan, MS^{1,2}, Amar Trivedi, MD³, Ann B. Ragin, PhD¹, James C. Carr, MD¹, Rod S. Passman, MD³, Daniel Kim, PhD^{1,2}

¹Department of Radiology, Northwestern University Feinberg School of Medicine, Chicago, IL, United States

²Department of Biomedical Engineering, Northwestern University, Evanston, IL, United States

³Division of Cardiology, Department of Internal Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL, United States

⁴Department of Radiology, Mayo Clinic, Rochester, MN, United States

Abstract

Introduction: A recent study reported diffuse left ventricular (LV) fibrosis is a predictor of atrial fibrillation (AF) recurrence following catheter ablation, by measuring post-contrast cardiac T₁ (an error prone metric as per the 2017 SCMR consensus statement) using an inversion-recovery pulse sequence (an error prone method in arrhythmia) in AF ablation candidates. The purpose of this study was to verify the prior study, by measuring extracellular volume fraction (ECV) (an accurate metric) using a saturation-recovery pulse sequence (accurate method in arrhythmia).

Methods and Results: This study examined 100 AF patients (mean age=62±11 years, 69 males and 31 females, 67 paroxysmal [pAF] and 33 persistent [peAF]) who underwent a pre-ablation cardiovascular magnetic resonance (CMR). LV ECV and LA and LV functional parameters were quantified using standard analysis methods. During an average follow-up period of 457±261 days with 4±3 rhythm checks per patient, 72 patients maintained sinus rhythm. Between those who maintained sinus rhythm (n=72) and those who reverted to AF (n=28), the only clinical characteristic that was significantly different was age (60 ± 12 years vs. 66 ± 9 years); for CMR metrics, neither mean LV ECV (25.1 ± 3.3% vs. 24.7±3.7%), native LV T₁ (1093.8 ± 73.5 ms vs. 1070.2 ± 115.9 ms), LVEF (54.1 ± 11.2% vs. 55.7±7.1%), or LA EDV/BSA (42.4 ± 14.8 mL/m² vs. 43.4±19.6 mL/m²) was not significantly different (p = 0.23). According to Cox regression tests, none of the clinical and imaging variables predicts AF recurrence.

Address for correspondence: Daniel Kim, 737 N. Michigan Ave, Suite 1600, Chicago, IL 60611, Fax: 312-926-5991, Phone: 312-926-1733, daniel.kim3@northwestern.edu.

Author Contributions

Suvai Gunasekaran and Daniel Kim contributed to this work by conceiving the study design, performing image and statistical analyses, drafting the paper, and approving the final version.

Daniel Lee, Bradley Knight, Jeremy Collins, Amar Trivedi, Lexiaozi Fan, Ann Ragin, James Carr, and Rod Passman contributed to this work by providing input to the study design, critically revising the manuscript, and approving the final version.

Lexiaozi Fan made an additional contribution to this work by performing data analysis.

Ann Ragin made an additional contribution to this work by providing assistance with statistical analysis.

Daniel Kim and Rod Passman made additional contribution to this work by securing funding support.

Conclusion: Neither LV ECV nor other CMR metrics predict recurrence of AF following catheter ablation.

Keywords

Atrial fibrillation; MRI; fibrosis; recurrence; risk stratification

Introduction

Atrial fibrillation (AF) affects between 2.7 to 6.1 million Americans and is the most prevalent arrhythmia (1). Catheter ablation is the best rhythm control treatment for AF but its success rates are only moderate: 70–80% for paroxysmal AF and < 70% for persistent AF (2, 3). Identifying accurate predictors based on clinical (e.g., AF duration, hypertension, sex, age) and imaging metrics (e.g., left atrial [LA] size, left ventricular [LV] function) for AF recurrence has proven difficult in clinical practice. LA fibrosis has been shown to be the arrhythmogenic substrate for initiating and maintaining AF (4–8). While LA fibrosis as assessed with 3D LA late gadolinium-enhanced (LGE) cardiovascular magnetic resonance (CMR) has shown promise to predict AF recurrence following catheter ablation (9–12), inadequate spatial resolution ($\sim 1.5 \text{ mm} \times 1.5 \text{ mm} \times 2.5 \text{ mm}$) of CMR for quantifying fibrosis in the thin ($\sim 1\text{--}2 \text{ mm}$) LA wall hinders its clinical translation.

One approach to overcoming the technical challenge of imaging the thin LA wall with CMR is to identify surrogate markers in the LV, since there is a complex relationship between the LA and LV in human AF pathophysiology. There are several mechanisms by which AF may impact the LV, including tachycardia (13, 14), atrial-ventricular dyssynchrony (15, 16), lack of atrial contraction (17, 18), functional mitral regurgitation (19, 20), and ventricular fibrosis (21). Given the aforementioned mechanisms, AF-mediated ventricular fibrosis, should it exist, is likely to be diffuse. A recent study by McLellan et al. (22) reported that diffuse LV fibrosis, as measured with post-contrast cardiac T_1 , predicts recurrence of AF following catheter ablation. We contend that the results from this study may have been influenced by the use of post-contrast cardiac T_1 as a marker of diffuse LV fibrosis, since post-contrast T_1 mapping is known to be sensitive to biological confounders such as the gadolinium clearance rate, time of measurement, body composition, and hematocrit and MRI-related confounders such as contrast agent type and dose and static magnetic field strength. To address these confounders, the CMR community has moved towards myocardial extracellular volume (ECV) fraction mapping (23, 24) instead, since, in the absence of myocardial edema, ECV demonstrates best overall agreement with published human histological validation studies (25). In addition, the results from the study by McLellan et al. (22) may have been influenced by use of an inversion-recovery based cardiac T_1 mapping pulse sequence, which is known to be sensitive to rapid heart rate and arrhythmia (26, 27). Due to both these biological and methodological confounders in McLellan et al. (22), another study accounting for the aforementioned confounders is warranted to investigate whether LV ECV expansion predicts recurrence of AF following catheter ablation.

Cardiac T_1 mapping in AF patients is technically challenging because of their irregular heart rhythm. For conventional inversion-recovery based pulse sequences such as Look Locker

inversion recovery (MOLLI)(28) and Shortened MOLLI (ShMOLLI)(29) in patients with arrhythmia, multiple T₁-weighted images would be sampled at different cardiac phases, making it difficult for a motion correction algorithm to align the images. In addition to the residual mis-alignment of images due to arrhythmia, beat-to-beat variations in magnetization recovery during arrhythmia will confound the Look-Locker correction for MOLLI and ShMOLLI. The first step to minimizing the sensitivity to arrhythmia is to achieve T₁-weighting with saturation recovery instead, which is commonly practiced in first-pass perfusion CMR (30). The second step is to require only a single T₁-weighted image for calculating T₁, thereby relaxing the motion correction problem. An arrhythmia-insensitive-rapid (AIR) cardiac T₁ mapping pulse sequence (26) is specifically designed with these two features to achieve insensitivity to arrhythmia; it was previously validated in large animals against histology (31) and evaluated in patients with sinus rhythm to show inferior precision than MOLLI (32).

In this observational study, we sought to overcome the methodological limitation experienced by McLellan et al. (22) and investigate whether LV ECV expansion, regardless of etiology, predicts recurrence of AF following catheter ablation, by accurately measuring ECV (improved metric) using AIR cardiac T₁ mapping (improved method).

Materials and Methods

Justification for AIR Cardiac T₁ mapping for Patients with AF

At our institution, AIR cardiac T₁ mapping replaced conventional MOLLI (28) T₁ mapping in the routine clinical CMR protocol for patients with AF, because MOLLI is known to produce inaccurate results in arrhythmia (26, 27).

Study Population

We identified 268 consecutive patients who underwent a pre-ablation clinical CMR at Northwestern Memorial Hospital from January 2017 to December 2018. The need for informed consent was waived. A retrospective study was approved by our Institutional Review Board (IRB) and was found to comply with the Health Insurance Portability and Accountability Act (HIPAA). 75 patients were excluded for not having AIR cardiac T₁ mapping; 10 were excluded for being imaged on a 3 Tesla scanner; 7 patients were excluded because they did not have follow-up rhythm status records available at our hospital; 38 patients were excluded because they had previously undergone an ablation procedure; 34 patients were excluded because they underwent radio-frequency (RF) ablation; 4 patients were excluded because they did not undergo an ablation procedure. Patients who did not undergo ablation had several reasons including having a thrombus in their left atrial appendage, a low hemoglobin level, or electing to continue antiarrhythmic drug treatment (amiodarone or tikosyn) instead of undergoing catheter ablation.

Patients with a history of coronary artery disease (CAD) was defined as significant coronary stenosis (left main >50% or major epicardial stenosis >70%) (33), a history of coronary revascularization, or prior myocardial infarction (MI); severe left ventricular hypertrophy (LVH) was defined as wall thickness > 1.5 cm (34). Each condition was determined based

on clinical chart review. We included all eligible patients, regardless of clinical history, except for those with a previous ablation procedure, as mentioned above.

MRI

CMR was performed on three 1.5 Tesla whole-body MRI scanners (MAGNETOM Aera & Avanto, Siemens Healthineers, Erlangen, Germany) equipped with a gradient system capable of achieving a maximum gradient strength of 45 mT/m and a slew rate of 200 T/m/s. Imaging was performed with body matrix and spine array coils with 18 and 32 coil elements on the Avanto and Aera, respectively.

The relevant imaging parameters for AIR cardiac T_1 mapping with balanced steady-state free precession readout are as follows: field of view = 400 mm $\times$ 300 mm, image acquisition matrix size = 192 $\times$ 144 (phase-encoding), spatial resolution = 2.1 mm $\times$ 2.1 mm, slice thickness = 8 mm, echo time (TE) = 1.1 ms, repetition time (TR) = 2.7 ms, receiver bandwidth = 930 Hz/pixel, flip angle = 55°, generalized autocalibrating partially parallel acquisitions (GRAPPA)(35) acceleration factor = 1.8, ECG triggering, linear k-space ordering, saturation-recovery time to center of k-space (TS) = 600 ms for native and 300 ms for post-contrast. The breath-hold duration (scan time) was 5 heart beats (one proton density weighted image during heart beat 1, 4 T_1 -weighted images during heart beats 2–5) per plane. This acquisition scheme enabled us to account for arrhythmia or respiratory motion by choosing one among 4 T_1 -weighted images that best registers with the proton density weighted image upon visual inspection. For each subject, we performed AIR cardiac T_1 mapping in two short-axis planes (base, mid) and one long-axis (4-chamber) plane. The apical short-axis plane was excluded due to its susceptibility to partial volume averaging around the endocardial border. Each patient received either 0.15 or 0.20 mmol/kg of gadobutrol (Gadavist, Bayer HealthCare Whippany, USA) via a power injector as part of the clinical protocol, depending whether the estimated glomerular filtrate rate (eGFR) was 45–59 or > 60 mL/min per 1.73 m², respectively. Post-contrast T_1 mapping was performed between 10–15 minutes after administration of gadobutrol, immediately after the clinical LGE scans.

Image Analysis

For assessment of LV ECV, first reader (SG, with 3 years of experience analyzing ECV and cardiac MRI) and second reader (LF, with 2 years of experience analyzing ECV and cardiac MRI) independently analyzed native T_1 and ECV maps, where ECV was calculated using the native and post-contrast T_1 , the difference in blood T_1 based on contours of LV cavity, and the patient's hematocrit, taken from the day of CMR scan, as per SCMR consensus statement (23, 24). The mean native T_1 and ECV values were calculated after manually drawing the endo- and epicardial contours. Using clinical LGE images covering the whole heart as a guide to determine areas of focal fibrosis, ROI for analysis were drawn only in areas without any focal fibrosis (e.g. myocardial infarction), since the focus of this study is LV ECV. The contour segmentation was performed using a customized tool developed in Matlab (R2017, The Mathworks Inc, Natick, MA, USA). Normal native myocardial T_1 was defined as 1233.7 ms, and normal ECV was defined as 32.8%. These cut points were calculated by the following process. In step 1, we calculated two standard deviations above

the norm of native T_1 (1102 ms) and ECV values (32.7%) derived from a prior study of 94 healthy volunteers (mean age = 50 ± 14 years; 49 males and 45 females) scanned with MOLLI cardiac T_1 mapping (36). In step 2, we applied linear models for converting MOLLI to AIR, as previously described (37). Presence of LGE were determined by the clinical radiology report. For estimating cardiac rhythm, the coefficient of variation of the R-R interval was used from a representative cine image set for each patient.

For assessment of LA end diastolic volume/body surface area (LA EDV/BSA), the first reader (SG) used CVI⁴² (Circle Cardiovascular Imaging Inc., Calgary, AB, Canada) to calculate maximum LA volume based on the area-length method (38), and BSA as determined based on the Mosteller formula. Normal LA EDV/BSA values were considered to be males 52.4 mL/m², females 53.4 mL/m² (39).

Catheter Ablation

All 100 patients underwent cryoballoon ablation (CB) (Artic Front Advance™, Medtronic, Minneapolis, MN). Standard procedures were used, including use of intracardiac echocardiography (AcuNav, Biosense Webster), fluoroscopy, and electroanatomic mapping (NavX, Abbott, and CARTO, Biosense Webster). Briefly, for CB, a minimum of two cryoablations were delivered per pulmonary vein (PV) with ablation lasting 3–4 minutes to a nadir temperature < 55°C. If PV isolation (PVI) was not achieved with CB, then focal ablation was performed using either cryocatheter (Cryocath, Medtronic) or radiofrequency catheter to achieve PVI. Entry block was confirmed by pacing from the distal poles of the coronary sinus catheter for the left sided PVs and elimination of right sided PVs. Exit block in all PVs was evaluated by pacing around the circular mapping catheter placed sequentially in each PV.

Rhythm Status following CB

Recurrence of AF was determined after a 3-month blanking period. A patient was classified as having a successful ablation if there was no recurrence of AF documented on medical chart review. AF recurrence was defined as any episodes of AF > 30 seconds off antiarrhythmic drugs. Rhythm status was determined using routine ECGs, Holter monitoring, or Zio patch monitoring (iRhythm Technologies, Inc, San Francisco, CA, USA) at multiple clinic visits.

Statistical Analysis

We used average readers' results for statistical analysis. Continuous variables were compared using a two-tailed, two-sample t-tests while categorical variables were compared using a two-tailed Fisher's exact test. AF recurrence was modeled using Cox Regression analysis; univariate predictors with a statistical significance were entered into a multivariate stepwise regression model. P-values < 0.05 were considered statistically significant for all analyses. Statistical analyses were performed using IBM SPSS Statistics for Windows (Version 23.0. Armonk, NY: IBM Corp).

Results

Baseline Clinical and CMR Variables

In total, we studied 100 patients (mean age = 62 ± 11 years, 79 males and 31 females, 67 (67%) paroxysmal AF) who underwent cryoballoon ablation. The mean coefficient of variation in the R-R interval during CMR for all patients was $10 \pm 10.4\%$. Table 1 lists patient characteristics for our cohort. For characteristics with at least 10 samples, significant differences were found for age, CHA₂DS₂-VASc, and number of previous cardioversions. Table 2 summarizes the CMR findings for our patient cohort. Both LA EDV/BSA (males 52.4 mL/m^2 , females 53.4 mL/m^2) and ECV (32.8%) was within the normal range for all AF groups, but both metrics were significantly ($p < 0.001$) higher for peAF than pAF. In our cohort, only 1 patient had ECV above the normal cut point (32.7%), but ECV ranged from 17.3 to 37.1%. While LVEF was within the normal range for all AF groups, it was significantly lower for peAF ($48.8 \pm 12.1\%$) than pAF ($57.4 \pm 7.9\%$). Focal fibrosis (as assessed with LGE CMR) was detected in 29 of patients, and there was no significant difference between the pAF and peAF groups.

Clinical and CMR Variables: Ablation Success vs. Failure

During an average follow-up period of 457 ± 261 days with 4 ± 3 rhythm checks per patient, 72 (72%) patients maintained sinus rhythm. While the success rate was higher in pAF patients (75%) than peAF patients (67%) (Table 1), the difference was not significantly different ($p = 0.48$). According to the two-sample t-test and Fisher's exact test comparing patients with and without recurrence of AF, none of the variables were significantly different except for age ($p = 0.22$) (Tables 3 and 4). According to the Cox regression model, none of the variables predicted AF recurrence in all patients (Table 5), pAF subgroup (Table 6), peAF subgroup (Table 7), or all patients without LGE (Table 8).

Discussion

The main finding of our study is that neither LV ECV expansion measured using AIR cardiac T₁ mapping nor other imaging metrics (see Table 4) predict recurrence of AF following catheter ablation. In our cohort of 100 patients, 72% of patients maintained sinus rhythm following catheter ablation, which is consistent with published success rates (2, 3, 40–43).

Our study contradicts the findings by McLellan et. al. who reported that diffuse LV fibrosis as measured with post-contrast T₁ predicts maintenance of sinus rhythm following catheter ablation (22). This discrepancy might be due to differences in patient population; our patients had less AF burden (shorter AF history and smaller LA volume) but higher co-morbidities (higher body mass index (BMI) and CHA₂DS₂-VASc). This discrepancy might be due to sensitivity of post-contrast cardiac T₁ mapping to confounders, including but not limited to renal function, type of contrast agent, and delaying time, and sensitivity of inversion-recovery based cardiac T₁ mapping to arrhythmia. In contrast, ECV measured with AIR cardiac T₁ mapping is insensitive to arrhythmia and the aforementioned confounders.

Our results also are inconsistent with the findings – LGE predicts AF recurrence - reported by Suksaranjit et. al. (44). In our patient population, the ablation success rate was similar between with (71%) and without (72%) LGE. The discrepancy might be due to differences in patient population (29% of our patients had positive LGE, of these positive LGE patients 20.7% was associated with CAD; 6.5% of their patients had positive LGE, of these positive LGE patients 46% was associated with CAD) and ablation modality (our cohort received cryoballoon ablation; their cohort received RF ablation).

Our findings have important clinical implications. First, while there is a complex relationship between the LA and LV in AF, it is likely that AF-mediated cardiomyopathy is a reversible condition (14) and not associated with diffuse LV fibrosis. While one prior study of a canine model with AF (3 months) reported the prevalence of diffuse LV fibrosis (21), another prior study of canine model with chronic AF (up to 22 months) contradicted that study and reported the absence of diffuse LV fibrosis (31). Our recent clinical study showed that LV ECV expansion is not associated with AF (37). Findings from this study agree with findings by Koopmann et al. (31) and Gunasekaran et al. (37). Second, LA fibrosis is the arrhythmogenic substrate for AF (4–8) and, thus, a better candidate for predicting AF recurrence following AF ablation. While it may have seemed like a plausible idea to overcome the technical challenge of imaging LA fibrosis with CMR by imaging LV ECV expansion as a surrogate predictor, our data suggest otherwise. Despite the technical difficulty, it is pathophysiologically more plausible to quantify LA fibrosis (i.e. substrate) using 3D LGE CMR for predicting AF recurrence (9–12). For wider clinical translation, it may be necessary to develop advanced 3D LA LGE CMR methods with higher spatial resolution, signal-to-noise ratio, and scanning efficiency, which may be possible by data acceleration techniques like extra motion-state Golden-angle Radial Sparse Parallel (XD-GRASP) (45) or higher magnetic field strength (≥ 3 Tesla).

This study has several limitations that warrant discussion. First, our sample size is relatively small with only 100 patients, but it is on par with 103 patients studied by McLellan et al. (22). A future study of a large AF cohort is warranted to adjust for confounders and test whether LV ECV expansion predicts AF recurrence following AF ablation. Second, post-ablation rhythm status checks were made clinically using a mixture of modalities (ECG, Holter monitor, and ZIO monitor) at multiple time points. However, we used all available rhythm status records, and any documentation of AF following the 3-month blanking period was defined as recurrence. Third, our patient population undergoing AF ablation at the Northwestern Memorial hospital had fewer women than men and fewer minorities (Blacks, Hispanics, or Asians) than Whites. Thus, it remains unclear whether the results from this study reflect AF pathophysiology in the general population. Fourth, LV ECV expansion was assessed from T_1 maps in 3 cardiac planes. While this approach is plausible for assessing LV ECV expansion, we acknowledge that 3 cardiac planes do not adequately reflect the whole heart. Fifth, success rates reported in this study reflects variations due to differences in skill level among ablationists. Sixth, this study did not conduct a head-to-head comparison between inversion-recovery based cardiac T_1 mapping used in McLellan et al. (22) and our AIR cardiac T_1 mapping. Inversion-based cardiac T_1 mapping pulse sequences are known to be sensitive to rapid heart rate and arrhythmia (26, 27). In contrast, our AIR cardiac T_1 mapping pulse sequence is insensitive to arrhythmia because it uses saturation-recovery and

only two (one proton density and one T₁ weighted) images are needed to produce a T₁ map. A future study is warranted to compare the sensitivity of both cardiac T₁ mapping pulse sequences, particularly in a large cohort, since as our study included only 100 patients and McLellan et al. (22) included only 103 patients.

In summary, neither diffuse LV fibrosis nor other image metrics (see Tables 4 and 5) predicted recurrence of AF following catheter ablation in our patient cohort. Thus, diffuse LV fibrosis, as measured by ECV, is likely a poor predictor of AF recurrence following cryoballoon ablation.

Acknowledgements

The authors thank funding support from the National Institutes of Health (R01HL116895, R01HL138578, R21EB024315, R21AG055954) and American Heart Association (14SFRN20480260, 19IPLOI34760317).

List of financial Support:

National Institutes of Health (R01HL116895, R01HL138578, R21EB024315, R21AG055954) and American Heart Association (14SFRN20480260, 19IPLOI34760317)

No relationships with industry

References

1. January CT, Wann LS, Alpert JS, Calkins H, Cigarroa JE, Cleveland JC Jr., et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. *J Am Coll Cardiol.* 2014;64(21):e1–76. [PubMed: 24685669]
2. Khan AR, Khan S, Sheikh MA, Khuder S, Grubb B, Moukarbel GV. Catheter ablation and antiarrhythmic drug therapy as first- or second-line therapy in the management of atrial fibrillation: systematic review and meta-analysis. *Circ Arrhythm Electrophysiol.* 2014;7(5):853–60. [PubMed: 25110162]
3. Wynn GJ, Das M, Bonnett LJ, Panikker S, Wong T, Gupta D. Efficacy of catheter ablation for persistent atrial fibrillation: a systematic review and meta-analysis of evidence from randomized and nonrandomized controlled trials. *Circ Arrhythm Electrophysiol.* 2014;7(5):841–52. [PubMed: 25132078]
4. Dzeshka MS, Lip GY, Snezhitskiy V, Shantsila E. Cardiac Fibrosis in Patients With Atrial Fibrillation: Mechanisms and Clinical Implications. *J Am Coll Cardiol.* 2015;66(8):943–59. [PubMed: 26293766]
5. Spragg D. Left Atrial Fibrosis: Role in Atrial Fibrillation Pathophysiology and Treatment Outcomes. *J Atr Fibrillation.* 2013;5(6):810. [PubMed: 28496835]
6. Tan AY, Zimetbaum P. Atrial fibrillation and atrial fibrosis. *J Cardiovasc Pharmacol.* 2011;57(6):625–9. [PubMed: 21633248]
7. Burstein B, Nattel S. Atrial fibrosis: mechanisms and clinical relevance in atrial fibrillation. *J Am Coll Cardiol.* 2008;51(8):802–9. [PubMed: 18294563]
8. Goldberger JJ, Arora R, Green D, Greenland P, Lee DC, Lloyd-Jones DM, et al. Evaluating the Atrial Myopathy Underlying Atrial Fibrillation: Identifying the Arrhythmogenic and Thrombogenic Substrate. *Circulation.* 2015;132(4):278–91. [PubMed: 26216085]
9. Mahnkopf C, Badger TJ, Burgon NS, Daccarett M, Haslam TS, Badger CT, et al. Evaluation of the left atrial substrate in patients with lone atrial fibrillation using delayed-enhanced MRI: implications for disease progression and response to catheter ablation. *Heart Rhythm.* 2010;7(10):1475–81. [PubMed: 20601148]
10. Oakes RS, Badger TJ, Kholmovski EG, Akoum N, Burgon NS, Fish EN, et al. Detection and quantification of left atrial structural remodeling with delayed-enhancement magnetic resonance

imaging in patients with atrial fibrillation. *Circulation*. 2009;119(13):1758–67. [PubMed: 19307477]

11. Akoum N, Daccarett M, McGann C, Segerson N, Vergara G, Kuppahally S, et al. Atrial fibrosis helps select the appropriate patient and strategy in catheter ablation of atrial fibrillation: a DE-MRI guided approach. *J Cardiovasc Electrophysiol*. 2011;22(1):16–22. [PubMed: 20807271]
12. McGann C, Akoum N, Patel A, Kholmovski E, Revelo P, Damal K, et al. Atrial fibrillation ablation outcome is predicted by left atrial remodeling on MRI. *Circ Arrhythm Electrophysiol*. 2014;7(1): 23–30. [PubMed: 24363354]
13. Patel JJ, Whittaker CT. Tachycardia-induced heart failure. *Perm J*. 2007;11(3):50–2.
14. Packer DL, Bardy GH, Worley SJ, Smith MS, Cobb FR, Coleman RE, et al. Tachycardia-induced cardiomyopathy: a reversible form of left ventricular dysfunction. *Am J Cardiol*. 1986;57(8):563–70. [PubMed: 3953440]
15. Abraham WT, Fisher WG, Smith AL, Delurgio DB, Leon AR, Loh E, et al. Cardiac resynchronization in chronic heart failure. *N Engl J Med*. 2002;346(24):1845–53. [PubMed: 12063368]
16. Auricchio A, Ding J, Spinelli JC, Kramer AP, Salo RW, Hoersch W, et al. Cardiac resynchronization therapy restores optimal atrioventricular mechanical timing in heart failure patients with ventricular conduction delay. *J Am Coll Cardiol*. 2002;39(7):1163–9. [PubMed: 11923041]
17. Timek T, Dagum P, Lai DT, Green GR, Glasson JR, Daughters GT, et al. The role of atrial contraction in mitral valve closure. *J Heart Valve Dis*. 2001;10(3):312–9. [PubMed: 11380093]
18. Keren G, Bier A, Sherez J, Miura D, Keefe D, LeJemtel T. Atrial contraction is an important determinant of pulmonary venous flow. *Journal of the American College of Cardiology*. 1986;7(3): 693–5. [PubMed: 3950247]
19. Gertz ZM, Raina A, Saghy L, Zado ES, Callans DJ, Marchlinski FE, et al. Evidence of atrial functional mitral regurgitation due to atrial fibrillation: reversal with arrhythmia control. *J Am Coll Cardiol*. 2011;58(14):1474–81. [PubMed: 21939832]
20. Delgado V, Bax JJ. Atrial Functional Mitral Regurgitation: From Mitral Annulus Dilatation to Insufficient Leaflet Remodeling. *Circ Cardiovasc Imaging*. 2017;10(3).
21. Avitall B, Bi J, Mykytsey A, Chicos A. Atrial and ventricular fibrosis induced by atrial fibrillation: evidence to support early rhythm control. *Heart Rhythm*. 2008;5(6):839–45. [PubMed: 18534368]
22. McLellan AJ, Ling LH, Azzopardi S, Ellims AH, Iles LM, Sellenger MA, et al. Diffuse ventricular fibrosis measured by T(1) mapping on cardiac MRI predicts success of catheter ablation for atrial fibrillation. *Circ Arrhythm Electrophysiol*. 2014;7(5):834–40. [PubMed: 25141860]
23. Messroghli DR, Moon JC, Ferreira VM, Grosse-Wortmann L, He T, Kellman P, et al. Clinical recommendations for cardiovascular magnetic resonance mapping of T1, T2, T2* and extracellular volume: A consensus statement by the Society for Cardiovascular Magnetic Resonance (SCMR) endorsed by the European Association for Cardiovascular Imaging (EACVI). *J Cardiovasc Magn Reson*. 2017;19(1):75. [PubMed: 28992817]
24. Moon JC, Messroghli DR, Kellman P, Piechnik SK, Robson MD, Ugander M, et al. Myocardial T1 mapping and extracellular volume quantification: a Society for Cardiovascular Magnetic Resonance (SCMR) and CMR Working Group of the European Society of Cardiology consensus statement. *J Cardiovasc Magn Reson*. 2013;15(1):92. [PubMed: 24124732]
25. Schelbert EB, Sabbah HN, Butler J, Gheorghiade M. Employing Extracellular Volume Cardiovascular Magnetic Resonance Measures of Myocardial Fibrosis to Foster Novel Therapeutics. *Circ Cardiovasc Imaging*. 2017;10(6):e005619. [PubMed: 28512159]
26. Fitts M, Breton E, Kholmovski EG, Dossdall DJ, Vijayakumar S, Hong KP, et al. Arrhythmia insensitive rapid cardiac T1 mapping pulse sequence. *Magn Reson Med*. 2013;70(5):1274–82. [PubMed: 23280998]
27. Gai N, Stehning C, Nacif M, Bluemke D. Modified Look-Locker T1 evaluation using Bloch simulations: Human and phantom validation. *Magnetic Resonance in Medicine*. 2012;DOI: 10.1002/mrm.24251.

28. Messroghli DR, Radjenovic A, Kozerke S, Higgins DM, Sivananthan MU, Ridgway JP. Modified Look-Locker inversion recovery (MOLLI) for high-resolution T1 mapping of the heart. *Magn Reson Med*. 2004;52(1):141–6. [PubMed: 15236377]
29. Piechnik SK, Ferreira VM, Dall'Armellina E, Cochlin LE, Greiser A, Neubauer S, et al. Shortened Modified Look-Locker Inversion recovery (ShMOLLI) for clinical myocardial T1-mapping at 1.5 and 3 T within a 9 heartbeat breathhold. *J Cardiovasc Magn Reson*. 2010;12:69. [PubMed: 21092095]
30. Tsekos NV, Zhang Y, Merkle H, Wilke N, Jerosch-Herold M, Stillman A, et al. Fast anatomical imaging of the heart and assessment of myocardial perfusion with arrhythmia insensitive magnetization preparation. *Magn Reson Med*. 1995;34(4):530–6. [PubMed: 8524020]
31. Koopmann M, Hong K, Kholmovski EG, Huang EC, Hu N, Ying J, et al. Post-contrast myocardial T(1) and ECV disagree in a longitudinal canine study. *NMR Biomed*. 2014;27(8):988–95. [PubMed: 24865566]
32. Hong K, Collins J, Lee DC, Wilcox JE, Markl M, Carr J, et al. Optimized AIR and investigational MOLLI cardiac T1 mapping pulse sequences produce similar intra-scan repeatability in patients at 3T. *NMR Biomed*. 2016;29(10):1454–63. [PubMed: 27593977]
33. Rosenthal RL. The 50% coronary stenosis. *Am J Cardiol*. 2015;115(8):1162–5. [PubMed: 25726382]
34. American College of Cardiology Foundation/American Heart Association Task Force on P, American Association for Thoracic S, American Society of E, American Society of Nuclear C, Heart Failure Society of A, Heart Rhythm S, et al. 2011 ACCF/AHA guideline for the diagnosis and treatment of hypertrophic cardiomyopathy: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Thorac Cardiovasc Surg*. 2011;142(6):e153–203. [PubMed: 22093723]
35. Griswold MA, Jakob PM, Heidemann RM, Nittka M, Jellus V, Wang J, et al. Generalized autocalibrating partially parallel acquisitions (GRAPPA). *Magn Reson Med*. 2002;47(6):1202–10. [PubMed: 12111967]
36. Rosmini S, Bulluck H, Captur G, Treibel TA, Abdel-Gadir A, Bhuva AN, et al. Myocardial native T1 and extracellular volume with healthy ageing and gender. *Eur Heart J Cardiovasc Imaging*. 2018;19(6):615–21. [PubMed: 29617988]
37. Gunasekaran S, Lee D, Knight B, Fan L, Collins J, Chow K, et al. Left ventricular extracellular volume expansion is not associated with atrial fibrillation or atrial fibrillation-mediated left ventricular systolic dysfunction. *Radiology: Cardiothoracic Imaging*. (in press).
38. Jiamsripong P, Honda T, Reuss CS, Hurst RT, Chaliki HP, Grill DE, et al. Three methods for evaluation of left atrial volume. *Eur J Echocardiogr*. 2008;9(3):351–5. [PubMed: 17658300]
39. Maceira AM, Cosin-Sales J, Roughton M, Prasad SK, Pennell DJ. Reference left atrial dimensions and volumes by steady state free precession cardiovascular magnetic resonance. *J Cardiovasc Magn Reson*. 2010;12:65. [PubMed: 21070636]
40. Takigawa M, Takahashi A, Kuwahara T, Okubo K, Takahashi Y, Watari Y, et al. Long-term follow-up after catheter ablation of paroxysmal atrial fibrillation: the incidence of recurrence and progression of atrial fibrillation. *Circ Arrhythm Electrophysiol*. 2014;7(2):267–73. [PubMed: 24610740]
41. Miyazaki S, Kuwahara T, Kobori A, Takahashi Y, Takei A, Sato A, et al. Long-term clinical outcome of extensive pulmonary vein isolation-based catheter ablation therapy in patients with paroxysmal and persistent atrial fibrillation. *Heart*. 2011;97(8):668–73. [PubMed: 20720249]
42. Brooks AG, Stiles MK, Laborderie J, Lau DH, Kuklik P, Shipp NJ, et al. Outcomes of long-standing persistent atrial fibrillation ablation: a systematic review. *Heart Rhythm*. 2010;7(6):835–46. [PubMed: 20206320]
43. Clarnette JA, Brooks AG, Mahajan R, Elliott AD, Twomey DJ, Pathak RK, et al. Outcomes of persistent and long-standing persistent atrial fibrillation ablation: a systematic review and meta-analysis. *Europace*. 2018;20(FI_3):f366–f76. [PubMed: 29267853]
44. Suksaranjit P, Akoum N, Kholmovski EG, Stoddard GJ, Chang L, Damal K, et al. Incidental LV LGE on CMR Imaging in Atrial Fibrillation Predicts Recurrence After Ablation Therapy. *JACC Cardiovasc Imaging*. 2015;8(7):793–800. [PubMed: 26093929]

45. Feng L, Axel L, Chandarana H, Block KT, Sodickson DK, Otazo R. XD-GRASP: Golden-angle radial MRI with reconstruction of extra motion-state dimensions using compressed sensing. *Magn Reson Med*. 2016;75(2):775–88. [PubMed: 25809847]

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 1.

Baseline patient characteristics and ablation success outcome comparisons based on AF types (paroxysmal vs. persistent). P-values were omitted for characteristics less than 10 samples.

	All (n = 100)	Paroxysmal (n = 67)	Persistent (n = 33)	P Value
Age (years)	62 ± 11	60 ± 12	65 ± 9	0.04*
Sex				
M	69 (69)	46 (69)	23 (70)	>0.99
F	31 (31)	21 (31)	10 (30)	
BMI	29.0 ± 5.94	28.8 ± 5.6	29.4 ± 6.2	0.62
Race				
White	96 (96)	63 (94)	33 (100)	0.30
African American	1 (1)	1 (2)	0 (0)	
Asian	2 (2)	2 (3)	0 (0)	
Hispanic	1 (1)	1 (2)	0 (0)	
CHA ₂ DS ₂ -VASc Score	2.1 ± 1.6	1.8 ± 1.5	2.7 ± 1.7	0.005*
AF duration (y)	2.9 ± 4.4	3.1 ± 4.6	2.5 ± 3.8	0.57
Previous Cardioversion	0.9 ± 1.2	0.6 ± 1.2	1.5 ± 1.2	< 0.001*
GFR (mL/min)	72.6 ± 20.1	73.9 ± 20.3	70.1 ± 19.6	0.34
Diabetes	11 (11)	7 (10)	4 (12)	0.83
Hypertension	52 (52)	34 (51)	18 (55)	
On ACE Inhibitor	17 (17)	12 (18)	5 (15)	
On ARB	14 (14)	10 (15)	4 (12)	>0.99
Coronary Artery Disease	15 (15)	7 (10)	8 (24)	0.08
Prior MI	8 (8)	3 (4)	5 (15)	0.48
Prior stent	7 (7)	5 (8)	2 (6)	
Prior CABG	3 (3)	0 (0)	3 (9)	
Severe LVH (≥ 15 mm)	7 (7)	5 (8)	2 (6)	0.48
Heart Failure	8 (8)	2 (3)	6 (18)	
Prior Stroke	9 (9)	5 (8)	4 (12)	
Ablation Success	72 (72)	50 (75)	22 (67)	0.48

BMI: body mass index, AF: atrial fibrillation, GFR: glomerular filtration rate, ACE: angiotensin-converting enzyme, ARB: angiotensin receptor blocker, MI: myocardial infarction, CABG: coronary artery bypass graft, LVH: left ventricular hypertrophy

Table 2.

Baseline CMR metrics comparisons based on AF type (paroxysmal vs. persistent). P-values were omitted for characteristics less than 10 samples.

	All (n = 100)	Paroxysmal (n = 67)	Persistent (n = 33)	P Value
LVEF (%)	54.6 ± 10.3	57.4 ± 7.9	48.8 ± 12.1	< 0.001*
LA EDV/BSA (mL/m ²)	42.7 ± 16.2	38.4 ± 14.6	47.8 ± 16.0	< 0.001*
Positive LGE	29 (29)	21 (31)	8(24)	0.49
Vascular	6 (6)	4 (6)	2 (6)	
ECV	25.0 ± 3.4	24.5 ± 3.1	26.1 ± 3.7	0.03*
Native Myocardial T ₁	1087.2 ± 87.5	1080.7 ± 92.8	1100.3 ± 75.3	0.29

LVEF: left ventricular ejection fraction, LA EDV/BSA: left atrial end diastolic volume/body surface area, LGE: late gadolinium enhancement, ECV: extracellular volume fraction

Table 3.

Patient characteristics comparisons based on rhythm status following catheter ablation. P-values were omitted for characteristics less than 10 samples.

	Maintained Sinus Rhythm (n = 72)	AF Recurrence (n = 28)	P Value
Age (years)	60 ± 12	66 ± 9	0.022*
Sex			
M	49 (68)	20 (71)	0.81
F	23 (32)	8 (29)	
BMI	29.1 ± 5.7	28.6 ± 6.6	0.69
Race			
White	68 (94)	28 (100)	0.57
African American	1 (1)	0 (0)	
Asian	2 (3)	0 (0)	
Hispanic	1 (1)	0 (0)	
CHA ₂ DS ₂ -VASc Score	2.0 ± 1.7	2.3 ± 1.5	0.48
AF Type			
Paroxysmal	50 (69)	17 (61)	0.47
Persistent	22 (31)	11 (39)	
AF Duration (y)	3.0 ± 4.8	2.7 ± 2.9	0.81
Previous Cardioversion	0.8 ± 1.3	1.0 ± 1.0	0.57
GFR (mL/min)	74.2 ± 20.4	68.5 ± 18.9	0.20
Diabetes	9 (13)	2 (7)	
Hypertension	33 (46)	19 (68)	0.074
On ACE Inhibitor	13 (18)	4 (14)	0.77
On ARB	9 (13)	5 (18)	
Coronary Artery Disease	10 (14)	5 (18)	0.76
Prior MI	5 (7)	3 (11)	
Prior stent	4 (6)	3 (11)	
Prior CABG	3 (4)	0 (0)	
Severe LVH (> 15 mm)	4 (6)	3 (11)	
Heart Failure	4 (6)	4 (14)	
Prior Stroke	7 (10)	2 (7)	

BMI: body mass index, AF: atrial fibrillation, GFR: glomerular filtration rate, ACE: angiotensin-converting enzyme, ARB: angiotensin receptor blocker, MI: myocardial infarction, CABG: coronary artery bypass graft, LVH: left ventricular hypertrophy

Table 4.

CMR metrics comparisons based on rhythm status following catheter ablation. P-values were omitted for characteristics less than 10 samples.

	Maintained Sinus Rhythm (n = 72)	AF Recurrence (n = 28)	P Value
LVEF (%)	54.1 ± 11.2	55.7 ± 7.1	0.49
LA EDV/BSA (mL/m ²)	42.4 ± 14.8	43.4 ± 19.6	0.77
Positive LGE	21 (29)	8 (29)	>0.99
Vascular	4 (6)	2 (7)	
ECV	25.1 ± 3.3	24.7 ± 3.7	0.57
Native Myocardial T ₁	1093.8 ± 73.5	1070.2 ± 115.9	0.23

LVEF: left ventricular ejection fraction, LA EDV/BSA: left atrial end diastolic volume/body surface area, LGE: late gadolinium enhancement, ECV: extracellular volume fraction

Table 5.

Cox regression analysis for predicting recurrence of AF following catheter ablation.

Variable	Hazard Ratio (HR)	95.0% CI for HR		P Value
		Lower	Upper	
Age	1.037	0.995	1.080	0.086
Previous Cardioversion	1.104	0.789	1.369	0.783
AF Type	1.171	0.548	2.504	0.683
AF Duration	0.986	0.901	1.080	0.764
LGE	0.954	0.419	2.172	0.911
Vascular LGE	0.729	0.171	3.099	0.668
LA EDV/BSA	1.009	0.986	1.032	0.466
LVEF	1.017	0.982	1.053	0.355
CHA ₂ DS ₂ -VASc	0.965	0.762	1.223	0.769
ECV	0.964	0.857	1.085	0.548
Native Myocardial T ₁	0.998	0.995	1.002	0.376

The hazard ratio reflects the Cox proportional hazard ratio of AF recurrence. AF: atrial fibrillation, LGE: late gadolinium enhancement, LA EDV/BSA: left atrial end diastolic volume/body surface area, LVEF: left ventricular ejection fraction, ECV: extracellular volume fraction

Table 6.

Cox regression analysis for predicting recurrence of AF following catheter ablation in patients with paroxysmal AF (n = 67).

Variable	Hazard Ratio (HR)	95.0% CI for HR		P Value
		Lower	Upper	
Age	1.051	0.992	1.113	0.092
Previous Cardioversion	1.029	0.705	1.503	0.881
AF Duration	1.007	0.914	1.108	0.894
LGE	1.542	0.584	4.072	0.382
Vascular LGE	1.227	0.276	5.456	0.788
LA EDV/BSA	1.002	0.968	1.037	0.923
LVEF	0.995	0.941	1.051	0.852
CHA ₂ DS ₂ -VASc	1.108	0.825	1.487	0.497
ECV	0.940	0.798	1.108	0.463
Native Myocardial T ₁	0.998	0.994	1.002	0.242

The hazard ratio reflects the Cox proportional hazard ratio of AF recurrence. AF: atrial fibrillation, LGE: late gadolinium enhancement, LA EDV/BSA: left atrial end diastolic volume/body surface area, LVEF: left ventricular ejection fraction, ECV: extracellular volume fraction

Table 7.

Cox regression analysis for predicting recurrence of AF following catheter ablation in patients with persistent AF (n = 33).

Variable	Hazard Ratio (HR)	95.0% CI for HR		P Value
		Lower	Upper	
Age	1.016	0.952	1.085	0.633
Previous Cardioversion	1.012	0.613	1.671	0.962
AF Duration	0.922	0.738	1.153	0.477
LGE	0.269	0.034	2.112	0.212
Vascular LGE	0.969	0.884	1.062	0.500
LA EDV/BSA	1.017	0.979	1.055	0.386
LVEF	1.049	0.994	1.107	0.084
CHA ₂ DS ₂ -VASc	0.716	0.464	1.105	0.131
ECV	0.976	0.816	1.167	0.789
Native Myocardial T ₁	1.000	0.992	1.009	0.941

The hazard ratio reflects the Cox proportional hazard ratio of AF recurrence. AF: atrial fibrillation, LGE: late gadolinium enhancement, LA EDV/BSA: left atrial end diastolic volume/body surface area, LVEF: left ventricular ejection fraction, ECV: extracellular volume fraction

Table 8.

Cox regression analysis for predicting recurrence of AF following catheter ablation in patients without LGE (n = 71).

Variable	Hazard Ratio (HR)	95.0% CI for HR		P Value
		Lower	Upper	
Age	1.040	0.994	1.088	0.089
Previous Cardioversion	1.063	0.797	1.418	0.677
AF Type	1.731	0.720	4.162	0.220
AF Duration	0.999	0.884	1.130	0.990
LA EDV/BSA	1.027	0.999	1.055	0.059
LVEF	1.013	0.968	1.059	0.581
CHA ₂ DS ₂ -VASc	0.936	0.703	1.246	0.817
ECV	0.984	0.857	1.129	0.817
Native Myocardial T ₁	0.997	0.992	1.003	0.341

The hazard ratio reflects the Cox proportional hazard ratio of AF recurrence. AF: atrial fibrillation, LGE: late gadolinium enhancement, LA EDV/BSA: left atrial end diastolic volume/body surface area, LVEF: left ventricular ejection fraction, ECV: extracellular volume fraction