Diffuse Ventricular Fibrosis Measured by $T_1$ Mapping on Cardiac MRI Predicts Success of Catheter Ablation for Atrial Fibrillation

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Background—There is a complex interplay between the atria and ventricles in atrial fibrillation (AF). Cardiac magnetic resonance (CMR) imaging provides detailed tissue characterization, identifying focal ventricular fibrosis with late gadolinium enhancement (ventricular late gadolinium enhancement) and diffuse fibrosis with postcontrast-enhanced $T_1$ mapping. The aim of the present study was to investigate the relationship between postcontrast ventricular $T_1$ relaxation time on CMR and freedom from AF after pulmonary vein isolation.

Methods and Results—One hundred three patients undergoing catheter ablation for symptomatic AF (66% paroxysmal AF; age, 58±10 years; left atrial area, 27±7 cm$^2$) underwent preprocedure CMR to determine postcontrast ventricular $T_1$ time. Follow-up included clinical review and 7-day Holter monitors at 6 monthly intervals. All patients underwent successful pulmonary vein isolation. At a mean follow-up of 15±7 months, the single procedure success was 74%. Postcontrast ventricular $T_1$ time was significantly shorter in patients with recurrent AF (366±73 ms) versus patients without AF recurrence (428±90 ms; $P=0.002$). Univariate predictors of AF recurrence included postcontrast ventricular $T_1$ time, AF type (paroxysmal versus persistent), AF duration, and body mass index. After multivariate analysis, ventricular $T_1$ time ($P=0.03$) and AF duration ($P=0.03$) were the only independent predictors. Freedom from AF was present in 84% of patients with a postcontrast ventricular $T_1$ time $>380$ ms versus 56% in patients with a postcontrast ventricular $T_1$ time $<380$ ms ($P=0.002$).

Conclusions—A shorter postcontrast ventricular $T_1$ relaxation time on CMR is associated with reduced freedom from AF after catheter ablation. Diffuse ventricular fibrosis as demonstrated by CMR may, in part, explain recurrent AF after AF ablation. (Circ Arrhythm Electrophysiol. 2014;7:834-840.)

Key Words: atrial fibrillation ■ fibrosis ■ magnetic resonance imaging

Clinical Perspective on p 840

Recurrent atrial fibrillation (AF) after catheter ablation remains an ongoing challenge, despite advances in technology and operator experience. A wide range of clinical and imaging predictors of recurrence has been previously identified. These include AF duration and type, left atrial (LA) size, left ventricular (LV) function, hypertension, and age among others.$^{1,3}$

We have recently demonstrated an independent association between the occurrence of diffuse ventricular fibrosis on cardiac magnetic resonance (CMR) as identified by $T_1$ mapping and the presence of AF.$^4$ CMR imaging with gadolinium contrast may demonstrate 2 patterns of ventricular fibrosis: focal scar with late gadolinium enhancement (LGE) or diffuse fibrosis on contrast-enhanced $T_1$ mapping sequences. LGE is qualitative and requires different signal intensity between fibrotic and normal tissue to generate imaging contrast,$^3$ however is insensitive to diffuse fibrosis. CMR with contrast-enhanced $T_1$ mapping has the ability to demonstrate diffuse myocardial fibrosis in the LV and is supported by histological validation in multiple independent studies.$^{5,6}$

AF may have detrimental effects on the ventricle secondary to rapid ventricular rates, irregular contraction, and the loss of atrial systole. Alternatively, diffuse ventricular fibrosis has also been described in the presence of many of the above conditions associated with AF recurrence such as ageing,$^7$ cardiomyopathy,$^8$ and hypertensive heart disease.$^9$

In the current study, we investigated whether the demonstration of diffuse ventricular fibrosis identified by CMR $T_1$...
mapping would independently predict patients at higher risk of AF recurrence after catheter ablation.

Methods

Study Population

Patients with symptomatic AF resistant to ≥1 antiarrhythmic medication were prospectively recruited before catheter ablation and underwent CMR with contrast enhancement and T₁ mapping between July 2009 and January 2013 at the Alfred Hospital. AF was classified as paroxysmal if episodes were self-terminating within 7 days or cardioverted within 48 hours of onset or persistent if episodes lasted >7 days or cardiovascular used after 48 hours of AF onset. Patients were required to have normal renal function and have no history of claustrophobia or metallic implant regarding contraindications for MRI. Baseline demographics including sex, age, height, weight, renal function, background medical conditions (hypertension, diabetes mellitus, ischemic heart disease, or heart failure [CCF]), and medications including failed antiarrhythmic drugs were recorded. The study was approved by the Alfred Hospital Human Research and Ethics Committee, and all patients gave informed consent.

CMR Protocol

The CMR protocol has been previously described and validated by our institution. Participants underwent CMR using a clinical 1.5-T MRI scanner (Signa HD 1.5-T, GE Healthcare, Waukesha, WI). Sequences were acquired during breath-holds of ≤15 seconds. LV function was assessed by a steady state free precession pulse sequence as previously described. Ventricular LGE was obtained 10 minutes after a bolus (0.2 mmol/kg body weight to a maximum of 20 mmol) of gadolinium-diethylene triamine penta-acetic acid (Magnevist, Schering, Berlin, Germany) to identify regional fibrosis using an inversion recovery gradient echo technique, where ventricular LGE was classified quantitatively by myocardial postcontrast signal intensity ≥2 SD above that within a reference region of remote myocardium. The T₁ mapping sequences were analyzed offline using a dedicated software enabled analysis of regions of interest to determine pixel by pixel relating the sample magnetization Mz observed at time t=TI to the equilibrium magnetization M₀ and sample T₁, where TI denotes inversion time for an inversion recovery experiment. For each image, a region of interest was drawn around the LV in mid short axis to calculate postcontrast ventricular T₁ time for each subject. Areas of regional ventricular LGE were excluded from the region of interest for T₁ measurement. The postcontrast ventricular T₁ time was corrected for height, weight, glomerular filtration rate (GFR) (standardized to 90 mL/min), and acquisition time postcontrast of the T₁ mapping sequence (standardized to 15 minutes) using a formula previously described by Gai et al. To exclude contrast kinetics as a confounding factor in the analysis of postcontrast myocardial T₁ time, postcontrast T₁ time was determined for the LA blood pool using a region of interest traced within the LA endocardial border. All T₁ measurements were made by a cardiologist with CMR expertise blinded to the clinical outcome.

Catheter Ablation

Catheter ablation involved anterolateral circumferential pulmonary vein isolation as described previously. In brief, all antiarrhythmic medications were stopped 5 half-lives preprocedure except amiodarone, which was ceased 2 weeks before the procedure. Warfarin was continued uninterrupted periprocedurally in patients already on warfarin. The procedures were performed under general anesthetic with an intraoperative transesophageal echocardiogram to rule out intracardiac thrombus. A decapolar catheter was positioned in the coronary sinus, and a quadripolar catheter was positioned in the His bundle position via femoral venous access. Two 8F or 8.5F long sheaths were introduced into the LA with transseptal puncture performed with a Brockenbrough needle (BRK-1; St. Jude Medical) under fluoroscopy and trans-esophageal echocardiogram guidance. A circular mapping catheter was introduced through the SL1 sheath into the LA for electric mapping of the pulmonary veins, and patients were given therapeutic heparin. Ablation was performed with an irrigated ablation catheter (4 mm, D curve, Navistar Thermocool and Thermocool, Biosense Webster or Coolflex, St. Jude Medical) using a dragging approach with a minimum duration of 30 seconds at each site or until separation or attenuation of the local electrogram at a maximum power 30 W reduced to 25 W on the posterior wall. An electroanatomic mapping system was used to guide ablation; NavX (St. Jude Medical) in 77% of patients or CARTO3 (Biosense Webster) in 23% of patients. Pulmonary vein isolation was achieved through ipsilateral circumferential antral ablation and was defined by pulmonary vein entrance block. If AF continued, patients underwent direct current cardioversion to restore sinus rhythm. Pulmonary vein exit block was confirmed, and an LA roof line (30 W) was completed with conduction block demonstrated by a corridor of widely spaced double potentials and caudocranial LA posterior wall activation during LA appendage pacing. Pulmonary vein isolation was confirmed 30 minutes after initial isolation including 2 challenges with intravenous adenosine 18 mg to assess for acute reconnection. Patients with a prior history of atrial flutter underwent cavitricuspid isthmus ablation with bidirectional block confirmed by differential pacing techniques.

Follow-Up

Procedural success was defined as freedom from any atrial arrhythmia after an initial 3-month blanking period. Recurrence was defined as any documented sustained atrial arrhythmia lasting >30 seconds in keeping with consensus guidelines. Postprocedure patients were followed-up in clinic at 1, 3, 6, and 12 months with ongoing review at 6 monthly intervals. Patients underwent a 7-day Holter monitor at 6 monthly intervals. Participants with recurrent symptoms were given instructions to contact the arrhythmia unit for immediate assessment and an event monitor.

Statistics

Continuous variables are expressed as a mean±SD with comparisons between groups performed with either an unpaired Student t test or where a normal distribution could not be assumed the Mann–Whitney U test. Categorical variables are expressed as numbers and percentages and were compared with a χ² test. AF recurrence was assessed with
Cox Regression analysis in univariate and multivariate models; univariate predictors with a significance <0.05 were entered into a multivariate stepwise regression model using P<0.05 for multivariate significance. Receiver operating characteristic curve analysis was performed across a range of ventricular T1 times to identify the best performing ventricular T1 relaxation time cutoff, and subsequently Kaplan–Meier analysis was performed to assess this cutoff on AF recurrence. A 2-sided P<0.05 was considered statistically significant. All statistical analysis was performed using SPSS software version 21.0 (SPSS, Chicago, IL).

Results

Baseline Characteristics

Baseline characteristics are presented in Table 1. One hundred three patients were prospectively recruited (66% paroxysmal AF; age, 57.7±10.2 years; male, 78%; AF duration, 4.5 years [range, 0.5–18 years]; LA area, 26.7±6.8 cm²; LV ejection fraction, 58.2±8.7%; hypertension, 35%; ischemic heart disease, 12%; CCF, 18%).

CMR Findings

CMR findings are presented in Table 2. The cohort had mildly dilated LA (LA area, 26.7±6.8 cm²; LA volume indexed to body surface area, 49.1±20.8 mL/m²), with normal LV size, function, and mass (left ventricular end-diastolic volume, 166.0±46.1 mL; left ventricular end-systolic volume, 69.8±26.2 mL; LV ejection fraction, 58.2±8.7%; LV mass index, 55.1±15.8 g/m²).

CMR Findings: Ventricular LGE

Ventricular LGE was present in 9 patients, with a higher rate in patients with persistent AF compared with patients with paroxysmal AF (17% versus 4%; P=0.03; Table 2). There was no significant difference in the presence of ventricular LGE between patients with and without recurrent AF postprocedure (Table 3).

Catheter Ablation

Results of catheter ablation are presented in Table I in the Data Supplement. Acute procedural success defined as pulmonary vein isolation achieved in all patients. A roof line was performed in 25%, and conduction block achieved in all. Cavotricuspid isthmus ablation was performed in 9% with bidirectional block confirmed by differential pacing techniques.

Follow-Up

At median follow-up of 13 months (Q1–Q3: 11–20 months), 76 of 103 (74%) patients were in sinus rhythm off antiarrhythmic medication. After a single procedure, AF recurred in 13 of 68 (19%) patients with paroxysmal AF and in 14 of 35 (40%) patients with persistent AF (P=0.025). Repeat catheter ablation was performed in 12 patients (12%).

Impact of Ventricular T1 Relaxation Time on AF Recurrence

Ventricular postcontrast T1 time was significantly shorter in patients with recurrent AF postprocedure compared with those with no recurrence (366±73 versus 428±90 ms in patients without AF recurrence; P=0.002). On Cox regression analysis, univariate predictors of AF recurrence included postcontrast ventricular T1 time (P=0.005), AF group (paroxysmal versus persistent; P=0.025), AF duration preablation (P=0.041), and body mass index (BMI; P=0.046). On multivariate analysis, postcontrast ventricular T1 time (P=0.031) and AF duration (P=0.028) were the only independent predictors (Table 4).

Receiver operating characteristic curve analysis was performed across a range of postcontrast ventricular T1 relaxation times, identifying a ventricular T1 time of 380 ms as the best performing ventricular T1 cutoff. Kaplan–Meier analysis revealed freedom from AF in 84% of patients with a postcontrast ventricular T1 time >380 ms versus 56% in patients with a postcontrast ventricular T1 time <380 ms (P=0.002; Figure).

After excluding patients with ventricular LGE (n=9), univariate predictors of AF recurrence on Cox regression analysis were ventricular T1 time (P=0.005), AF group (P=0.01), and BMI

Table 1. Baseline Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Paroxysmal (n=68)</th>
<th>Persistent (n=35)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>58.2±10.2</td>
<td>56.8±10.4</td>
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</tr>
<tr>
<td>Sex, male n (%)</td>
<td>50 (74)</td>
<td>30 (86)</td>
<td>0.16</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.6±3.6</td>
<td>27.6±4.2</td>
<td>0.99</td>
</tr>
<tr>
<td>GFR, mL/min</td>
<td>89.4±13.3</td>
<td>89.5±16.8</td>
<td>0.98</td>
</tr>
<tr>
<td>LA area (cm²)</td>
<td>24.7±5.7</td>
<td>30.7±7.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AF duration (years)</td>
<td>4.3±3.8</td>
<td>5.0±4.4</td>
<td>0.40</td>
</tr>
<tr>
<td>CHADS2-VaSc</td>
<td>1.1±1.1</td>
<td>1.4±1.1</td>
<td>0.16</td>
</tr>
<tr>
<td>Hypertension</td>
<td>22 (32)</td>
<td>14 (40)</td>
<td>0.44</td>
</tr>
<tr>
<td>IHD</td>
<td>6 (9)</td>
<td>6 (17)</td>
<td>0.21</td>
</tr>
<tr>
<td>CCF or ARB</td>
<td>5 (7)</td>
<td>14 (40)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Aldosterone antagonist</td>
<td>2 (3)</td>
<td>6 (17)</td>
<td>0.05</td>
</tr>
<tr>
<td>Number of failed AAD</td>
<td>1.4±0.7</td>
<td>1.6±0.6</td>
<td>0.45</td>
</tr>
</tbody>
</table>

AAD indicates antiarrhythmic drugs; ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; GFR, glomerular filtration rate; IHD, ischemic heart disease; and LA, left atrial.

Table 2. CMR Characteristics

<table>
<thead>
<tr>
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<th>Paroxysmal (n=68)</th>
<th>Persistent (n=35)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LA area (cm²)</td>
<td>24.7±5.7</td>
<td>30.7±7.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LA volume (mL)</td>
<td>91.5±40.9</td>
<td>116.8±40.1</td>
<td>0.003</td>
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<tr>
<td>LV mass (mL/m²)</td>
<td>45.2±20.7</td>
<td>56.5±19.1</td>
<td>0.003</td>
</tr>
<tr>
<td>LVESV (mL)</td>
<td>163±49</td>
<td>172±40</td>
<td>0.35</td>
</tr>
<tr>
<td>LVESV (mL/m²)</td>
<td>79.1±24.3</td>
<td>83.3±18.8</td>
<td>0.38</td>
</tr>
</tbody>
</table>

AF indicates atrial fibillation; BSA, body surface area; CMR, cardiac magnetic resonance; LA, left atrial; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; and LVESV, left ventricular end-systolic volume.
Table 3. Patient and CMR Characteristics: AF Recurrence After Ablation

<table>
<thead>
<tr>
<th></th>
<th>No AF Recurrence (n=76)</th>
<th>AF Recurrence (n=27)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>57.1±10.4</td>
<td>59.3±9.7</td>
<td>0.34</td>
</tr>
<tr>
<td>Sex: male, n (%)</td>
<td>62 (82)</td>
<td>18 (67)</td>
<td>0.11</td>
</tr>
<tr>
<td>Paroxysmal AF, n (%)</td>
<td>55 (72)</td>
<td>13 (48)</td>
<td>0.02</td>
</tr>
<tr>
<td>AF duration, y</td>
<td>4.0±3.8</td>
<td>5.9±4.2</td>
<td>0.03</td>
</tr>
<tr>
<td>AF at time of baseline CMR</td>
<td>17 (22)</td>
<td>8 (30)</td>
<td>0.45</td>
</tr>
<tr>
<td>Heart rate (if in sinus rhythm at baseline CMR)</td>
<td>63.1±13.0</td>
<td>66.9±12.9</td>
<td>0.99</td>
</tr>
<tr>
<td>Heart rate (if in AF at baseline CMR)</td>
<td>80.4±13.5</td>
<td>82.9±11.4</td>
<td>0.67</td>
</tr>
<tr>
<td>GFR, mL/min</td>
<td>90.3±14.3</td>
<td>88.6±15.0</td>
<td>0.28</td>
</tr>
<tr>
<td>BMI</td>
<td>27.2±3.9</td>
<td>28.9±3.1</td>
<td>0.04</td>
</tr>
<tr>
<td>HT</td>
<td>23 (30)</td>
<td>13 (48)</td>
<td>0.09</td>
</tr>
<tr>
<td>CCF</td>
<td>12 (16)</td>
<td>7 (26)</td>
<td>0.24</td>
</tr>
<tr>
<td>IHD</td>
<td>8 (11)</td>
<td>4 (15)</td>
<td>0.55</td>
</tr>
<tr>
<td>LA area, cm²</td>
<td>26.2±5.7</td>
<td>28.3±5.5</td>
<td>0.18</td>
</tr>
<tr>
<td>LA volume, mL</td>
<td>98.2±46.9</td>
<td>105.3±24.3</td>
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<tr>
<td>LA volume/BSA, mL/m²</td>
<td>48.5±23.4</td>
<td>50.7±10.7</td>
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<tr>
<td>LVEDV, mL</td>
<td>166.4±46.3</td>
<td>164.9±46.3</td>
<td>0.89</td>
</tr>
<tr>
<td>LVEDV/BSA, mL/m²</td>
<td>81.1±23.7</td>
<td>79.0±19.5</td>
<td>0.68</td>
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<tr>
<td>LVEF</td>
<td>58.9±8.8</td>
<td>56.1±8.3</td>
<td>0.16</td>
</tr>
<tr>
<td>LV mass, g</td>
<td>111.8±29.3</td>
<td>117.1±34.2</td>
<td>0.44</td>
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<tr>
<td>LV mass/BSA, g/m²</td>
<td>54.7±15.8</td>
<td>56.4±16.0</td>
<td>0.64</td>
</tr>
<tr>
<td>Regional LV-delayed enhancement</td>
<td>7 (9)</td>
<td>2 (7)</td>
<td>0.78</td>
</tr>
<tr>
<td>Ventricular T₁ relaxation time</td>
<td>427.9±90.1</td>
<td>366.0±72.6</td>
<td>0.002</td>
</tr>
<tr>
<td>Blood pool T₁ relaxation time</td>
<td>247.7±38.7</td>
<td>238.7±26.1</td>
<td>0.26</td>
</tr>
</tbody>
</table>

AF indicates atrial fibrillation; BMI, body mass index; BSA, body surface area; CMR, cardiac magnetic resonance; GFR, glomerular filtration rate; HT, hypertension; IHD, ischemic heart disease; LA, left atrial; LVEDV, left ventricular end-diastolic volume; and LVEF, left ventricular ejection fraction.

(P=0.04). After multivariate analysis, ventricular T₁ time was the only predictor (P=0.049; Table II in the Data Supplement).

After excluding patients (n=25) who were in AF at the time of baseline CMR, univariate predictors included ventricular T₁ time (P=0.008), LA area (P=0.013), BMI (P=0.035), AF duration (P=0.046), and AF group (P=0.043). On multivariate analysis, ventricular T₁ time (P=0.004), LA area (P=0.004), BMI (P=0.030), and AF duration (P=0.009) remained as significant predictors (Table III in the Data Supplement). Univariate and multivariate predictors of postcontrast ventricular T₁ time are presented in Table IV in the Data Supplement.

Discussion

The main finding of the study is that postcontrast ventricular T₁ relaxation time on CMR independently predicts freedom from recurrent AF after catheter ablation.

AF and Ventricular Fibrosis

Ventricular fibrosis may occur secondary to AF as a consequence of rapid ventricular rates, the irregularity of ventricular contraction or activation of the renin–angiotensin–aldosterone system. Alternatively, there are a range of clinical conditions such as hypertension, heart failure, obesity, and ageing which are associated with AF and a propensity to tissue fibrosis. Cardiac MRI with gadolinium contrast provides a noninvasive assessment of myocardial fibrosis with LGE representative of focal scar and postcontrast T₁ mapping sequences quantifying diffuse fibrosis. Postcontrast ventricular T₁ time provides a sensitive qualitative index of tissue as a measure of bimodal clinical variables.

Few studies provide histological evaluation of the ventricle in patients with AF. Frustaci et al performed LV endomyocardial biopsy in 14 patients with lone AF, demonstrating nonspecific necrosis or fibrosis in 60%. Kobayashi et al reported similar findings in 50 patients with supraventricular tachycardia, noting abnormal histopathology in two thirds of patients with AF.

We have previously demonstrated a progressive reduction in ventricular T₁ relaxation time in patients with persistent AF and paroxysmal AF compared with controls. In the present study, AF type was a predictor of procedural success; however, after multivariate analysis, postcontrast ventricular T₁ relaxation time and AF duration were the sole predictors of outcome.

Postcontrast ventricular T₁ relaxation time has been shown to shorten as diastolic function worsens. Diastolic dysfunction and LA stiffness as assessed on echocardiography have been associated with an increase in recurrent AF after catheter ablation. In the present study, shortening of the postcontrast ventricular T₁ time representative of tissue fibrosis may result in diastolic dysfunction, increased LA pressure and chronic atrial stretch, and fibrosis with the consequence of recurrent AF after catheter ablation. Alternatively, some patients may have an AF-mediated cardiomyopathy as opposed to diastolic dysfunction responsible for AF (the chicken and the egg).

CMR and AF

CMR is a well-established tool in the noninvasive assessment of patients with AF undergoing catheter ablation. Marrouche and coworkers have identified delayed enhancement within the atrium in patients with AF as predictive of outcome after catheter ablation. In patients with AF and LV dysfunction, an absence of ventricular delayed enhancement on CMR seems predictive of normalization of ventricular function after AF ablation. In the present study, LV LGE was present in just 9%, reflective of the low incidence of ischemic heart disease (12%) and heart failure (18%) in the study population. As such, the present study was underpowered to determine the impact of ventricular LGE on outcome after catheter ablation given its low incidence in our study.

AF Ablation: Predictors of Outcome

Recurrent arrhythmia after catheter ablation for AF remains important, despite increasing operator experience and evolution of mapping systems and ablation technologies. A range of conditions have been identified to predict recurrent AF after catheter ablation including nonparoxysmal AF, sleep apnoea, obesity, increased LA size, older age, hypertension, and LA fibrosis on cardiac MRI. In the present study, AF group and obesity (BMI) were identified as predictors of recurrent AF; however, LA size and older age were not predictive. This may be explained by patient selection for catheter ablation with a relatively younger...
age (mean 58±10 years) and smaller LA dimensions (LA area 27±7 cm²) in the study cohort. A meta-analysis that included 25 studies identified nonparoxysmal versus paroxysmal AF as the only predictive variable for recurrent AF after catheter ablation.2 Because we did not perform high resolution atrial delayed enhancement imaging, we were unable to provide a correlation between the degree of focal atrial fibrosis and AF recurrence as previously shown by Marrouche and coworkers.23

In the present study, receiver operating characteristic curves were assessed across a range of ventricular T₁ times to determine the best performing variable. The best performing ventricular T₁ time across the total study cohort was 380 ms (P=0.002). This is consistent with an earlier report by Sibley et al,6 who identified a cutoff of 383 ms as predictive of <5% ventricular fibrosis on endomyocardial biopsy.

Limitations
The present study used a histologically validated T₁ mapping technique; however, factors such as heart rate, GFR, and time of acquisition of the T₁ mapping sequence may affect the T₁ relaxation time.18 Comparing patients with and without AF at follow-up, there was no significant difference between these

### Table 4. Cox Regression Analysis

<table>
<thead>
<tr>
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<th>Univariate</th>
<th></th>
<th>Multivariate</th>
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<tbody>
<tr>
<td></td>
<td>Hazard Ratio (95% CI)</td>
<td>PValue</td>
<td>Hazard Ratio (95% CI)</td>
<td>PValue</td>
</tr>
<tr>
<td>AF group (paroxysmal vs persistent)</td>
<td>0.421 (0.197–0.896)</td>
<td>0.025</td>
<td>0.536 (0.247–1.166)</td>
<td>0.116</td>
</tr>
<tr>
<td>Age</td>
<td>1.018 (0.978–1.059)</td>
<td>0.382</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Sex</td>
<td>1.917 (0.861–4.268)</td>
<td>0.111</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>AF duration</td>
<td>1.085 (1.003–1.174)</td>
<td>0.041</td>
<td>1.097 (1.010–1.191)</td>
<td>0.028</td>
</tr>
<tr>
<td>BMI</td>
<td>1.083 (1.001–1.170)</td>
<td>0.046</td>
<td>1.057 (0.974–1.147)</td>
<td>0.185</td>
</tr>
<tr>
<td>IHD</td>
<td>0.817 (0.281–2.374)</td>
<td>0.710</td>
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<td>...</td>
</tr>
<tr>
<td>CCF</td>
<td>0.588 (0.248–1.392)</td>
<td>0.227</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.532 (0.250–1.134)</td>
<td>0.102</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>LA size</td>
<td>1.033 (0.982–1.086)</td>
<td>0.211</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>LA volume, mL</td>
<td>1.044 (0.983–1.109)</td>
<td>0.348</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>LV volume/BSA, mL/m²</td>
<td>0.997 (0.981–1.013)</td>
<td>0.728</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>LV mass/BSA, g/m²</td>
<td>1.005 (0.982–1.029)</td>
<td>0.650</td>
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<tr>
<td>LVEF</td>
<td>0.971 (0.932–1.011)</td>
<td>0.155</td>
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<tr>
<td>Ventricular T₁, relaxation time</td>
<td>0.994 (0.989–0.998)</td>
<td>0.005</td>
<td>0.995 (0.990–0.999)</td>
<td>0.031</td>
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<tr>
<td>Ventricular LGE</td>
<td>1.220 (0.289–5.154)</td>
<td>0.786</td>
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<tr>
<td>Procedure duration</td>
<td>1.007 (0.995–1.019)</td>
<td>0.253</td>
<td>...</td>
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</tr>
<tr>
<td>Radio-frequency ablation duration</td>
<td>1.018 (0.985–1.052)</td>
<td>0.294</td>
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<tr>
<td>Roof line</td>
<td>0.510 (0.233–1.114)</td>
<td>0.091</td>
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<td>...</td>
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<tr>
<td>Acute reconnection</td>
<td>1.360 (0.564–3.280)</td>
<td>0.494</td>
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The hazard ratio reflects the Cox proportional hazard ratio of AF recurrence. AF indicates atrial fibrillation; BMI, body mass index; BSA, body surface area; CI, confidence interval; IHD, ischemic heart disease; LA, left atrial; LGE, late gadolinium enhancement; and LVEF, left ventricular ejection fraction.

**Figure.** Kaplan–Meier curve: postcontrast ventricular T₁ time more or less than 380 ms.
parameters (Table 3). The reported T1 times were adjusted for confounders such as height, weight, GFR, and time at which the T1 sequence was performed. In addition, there was no significant difference in the blood pool T1 relaxation time in patients with and without AF recurrence, effectively excluding gadolinium contrast kinetics as a cause for the observed differences in ventricular T1 relaxation times (Table 3). We are unable to present data comparing the performance of noncontrast T1 times or extracellular volume calculation with postcontrast T1 times in the prediction of AF recurrence because these methods were not published at the time of commencement of our study. This would clearly be an area of interest for future research. We are unable to provide correlation of ventricular postcontrast T1 relaxation time with the presence of atrial LGE because atrial LGE could not be definitively identified in any patient.

AF was present during the baseline CMR in only 37% of patients with persistent AF and is reflective of using the strict definition of persistent AF according to Heart Rhythm Society consensus guidelines, and patients being selected for ablation if continuous AF duration was <2 years. Therefore, the present study may not apply to patients with more long standing AF with more advanced atrial disease. In addition, T1 mapping was not repeated in the same patient in AF, as well as in sinus rhythm because of limitations of MRI usage and budgetary considerations; however, the key findings of the study were unchanged after excluding patients in AF during CMR.

Conclusions
A shorter postcontrast ventricular T1 relaxation time on CMR is associated with reduced freedom from AF after catheter ablation. Diffuse ventricular fibrosis as demonstrated by CMR may, in part, explain recurrent AF after AF ablation. Ventricular T1 time may assist in guiding patient selection and ablation strategy for patients with AF.

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Disclosures
None.

References
CLINICAL PERSPECTIVE

Recurrent atrial fibrillation after catheter ablation is increased in patients with structural heart disease and hypertension. The presence of ventricular fibrosis may, in part, explain atrial fibrillation (AF) recurrence through increased atrial pressure and stretch. Cardiac magnetic resonance imaging provides detailed tissue characterization, identifying focal ventricular fibrosis with late gadolinium enhancement and diffuse ventricular fibrosis with postcontrast-enhanced T₁ mapping. Diffuse ventricular fibrosis was measured in 103 patients before AF ablation using postcontrast T₁ mapping on cardiac magnetic resonance. Recurrent AF was associated with a shorter postcontrast ventricular T₁ time (postcontrast ventricular T₁ time, 366±73 ms) compared with patients with freedom from AF (428±90 ms; P=0.002) at mean follow-up of 15±7 months. On Cox regression analysis, the postcontrast ventricular T₁ time and AF duration were the only multivariate predictors of freedom from AF. A postcontrast ventricular T₁ time of >380 ms was associated with freedom from AF in 84% versus 56% in patients with a T₁ time <380 ms (P=0.002). Diffuse ventricular fibrosis as demonstrated by cardiac magnetic resonance may, in part, explain recurrent AF after AF ablation. Ventricular T₁ mapping may assist in patient selection and guide ablation strategies in patients with atrial fibrillation.
Diffuse Ventricular Fibrosis Measured by $T_1$ Mapping on Cardiac MRI Predicts Success of Catheter Ablation for Atrial Fibrillation

Alex J.A. McLellan, Liang-han Ling, Sonia Azzopardi, Andris H. Ellims, Leah M. Iles, Michael A. Selleng, Joseph B. Morton, Jonathan M. Kalman, Andrew J. Taylor and Peter M. Kistler

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Supplementary Table 1:

Procedural Characteristics

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<th>Paroxysmal</th>
<th>Persistent</th>
<th>P value</th>
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<tr>
<td></td>
<td>n = 68</td>
<td>n = 35</td>
<td></td>
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<tr>
<td>Procedure time (min)</td>
<td>162±29</td>
<td>189±39</td>
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<tr>
<td>Fluoroscopy time (min)</td>
<td>25.3±9.8</td>
<td>27.9±9.2</td>
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<td>Radiation Dose (mGy/cm²)</td>
<td>41802±29231</td>
<td>66658±46325</td>
<td>0.01</td>
</tr>
<tr>
<td>Total RF time (min)</td>
<td>40.9±12.1</td>
<td>47.1±13.4</td>
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<td>PV isolation %</td>
<td>100</td>
<td>100</td>
<td>1.0</td>
</tr>
<tr>
<td>Cavo-tricuspid isthmus ablation n (%)</td>
<td>6 (9)</td>
<td>3 (9)</td>
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<td>Roof Line</td>
<td>2 (3)</td>
<td>24 (69)</td>
<td>&lt;0.001</td>
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<td>Acute reconnection</td>
<td>26 (41)</td>
<td>7 (23)</td>
<td>0.07</td>
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<tr>
<td>Freedom from AF at follow up*</td>
<td>55 (81)</td>
<td>21 (60)</td>
<td>0.02</td>
</tr>
<tr>
<td>Redo Procedure</td>
<td>6 (9)</td>
<td>6 (17)</td>
<td>0.21</td>
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</table>

*Freedom from AF after initial procedure
### Supplementary table 2:

**Cox regression analysis excluding patients with ventricular late gadolinium enhancement**

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<td>B</td>
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<td>B</td>
<td>P value</td>
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<td>AF group</td>
<td>-1.037</td>
<td>0.010</td>
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<td>(paroxysmal vs. persistent)</td>
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<tr>
<td>Age</td>
<td>0.022</td>
<td>0.298</td>
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<td>-</td>
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<tr>
<td>Gender</td>
<td>0.650</td>
<td>0.119</td>
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<tr>
<td>AF duration</td>
<td>0.062</td>
<td>0.149</td>
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<td>BMI</td>
<td>0.082</td>
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<td>0.039</td>
<td>0.345</td>
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<td>IHD</td>
<td>0.129</td>
<td>0.836</td>
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<td>CCF</td>
<td>0.714</td>
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<td>0.587</td>
<td>0.145</td>
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<tr>
<td>DM</td>
<td>-3.044</td>
<td>0.584</td>
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<tr>
<td>LA size</td>
<td>0.036</td>
<td>0.186</td>
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<td>LVEF</td>
<td>-0.032</td>
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<tr>
<td>Ventricular T₁ relaxation time</td>
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<td>0.005</td>
<td>-0.005</td>
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<td>Procedure Duration</td>
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Supplementary table 3:

Cox Regression analysis excluding patients in AF at time of baseline CMR

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<td>B</td>
<td>P value</td>
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<td>-0.428</td>
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<td>(paroxysmal vs. persistent)</td>
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<td>Age</td>
<td>0.021</td>
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<td>Heart rate during CMR</td>
<td>0.018</td>
<td>0.286</td>
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<td>Gender</td>
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<td>0.590</td>
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<tr>
<td>AF duration</td>
<td>0.089</td>
<td>0.046</td>
<td>0.142</td>
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<td>BMI</td>
<td>0.117</td>
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<td>IHD</td>
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<td>0.766</td>
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<td>LA size</td>
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<td>0.185</td>
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<tr>
<td>Acute Reconnection</td>
<td>-0.319</td>
<td>0.555</td>
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Supplementary table 4:

Univariate and multivariate predictors of post-contrast T1 relaxation time in the left ventricle

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<th>Multivariate Model</th>
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<td></td>
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<td>$R^2$</td>
<td>p value</td>
<td>B</td>
<td>SE B</td>
<td>$\beta$</td>
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<td>Age, years</td>
<td>0.85</td>
<td>0.01</td>
<td>0.36</td>
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<tr>
<td>Body mass index, kg/m$^2$</td>
<td>10.69</td>
<td>0.10</td>
<td>0.001</td>
<td>-5.32</td>
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<tr>
<td>Hypertension</td>
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<td>0.00</td>
<td>0.95</td>
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<td>-</td>
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<tr>
<td>AF category (persistent vs. paroxysmal)</td>
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<td>0.02</td>
<td>0.17</td>
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<td>0.82</td>
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<td>LA volume index</td>
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<td>0.01</td>
<td>0.48</td>
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<td>LV EF, %</td>
<td>11.54</td>
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<td>LV EDV index, ml/m$^2$</td>
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<td>LV mass index, g/m$^2$</td>
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<td>Beta-blocker</td>
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<td>0.00</td>
<td>0.82</td>
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Univariate and multivariate linear regression was used to assess predictors of post-contrast T$_1$ relaxation time in the left ventricle.