Cardiac magnetic resonance T1 mapping of left atrial myocardium

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BACKGROUND Cardiac magnetic resonance (CMR) T1 mapping is an emerging tool for objective quantification of myocardial fibrosis.

OBJECTIVES To (a) establish the feasibility of left atrial (LA) T1 measurements, (b) determine the range of LA T1 values in patients with atrial fibrillation (AF) vs healthy volunteers, and (c) validate T1 mapping vs LA intracardiac electrogram voltage amplitude measures.

METHODS CMR imaging at 1.5 T was performed in 51 consecutive patients before AF ablation and in 16 healthy volunteers. T1 measurements were obtained from the posterior LA myocardium by using the modified Look-Locker inversion-recovery sequence. Given the established association of reduced electrogram amplitude with fibrosis, intracardiac point-by-point bipolar LA voltage measures were recorded for the validation of T1 measurements.

RESULTS The median LA T1 relaxation time was shorter in patients with AF (387 [interquartile range 364–428] ms) compared to healthy volunteers (459 [interquartile range 418–532] ms; $P < .001$) and was shorter in patients with AF with prior ablation compared to patients without prior ablation ($P = .035$). In a generalized estimating equations model, adjusting for data clusters per participant, age, rhythm during CMR, prior ablation, AF type, hypertension, and diabetes, each 100-ms increase in T1 relaxation time was associated with 0.1 mV increase in intracardiac bipolar LA voltage ($P = .025$).

CONCLUSIONS Measurement of the LA myocardium T1 relaxation time is feasible and strongly associated with invasive voltage measures. This methodology may improve the quantification of fibrotic changes in thin-walled myocardial tissues.

KEYWORDS Atrial fibrillation; Cardiac magnetic resonance; T1 mapping; Left atrial fibrosis; Late gadolinium enhancement

ABBREVIATIONS **AF** = atrial fibrillation; **CI** = confidence interval; **CMR** = cardiac magnetic resonance; **GEE** = generalized estimating equation; **IQR** = interquartile range; **LA** = left atrial; **LGE-CMR** = late gadolinium enhancement on cardiac magnetic resonance; **LV** = left ventricular; **PVAI** = pulmonary vein antral isolation; **ROI** = region of interest

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Introduction

Atrial fibrillation (AF) is the most common arrhythmia, affects 1%–1.5% of the population and up to 10% of the elderly,[1] and is associated with significant morbidity and mortality.[2] Many studies highlight an association between atrial fibrosis and AF.[3–5] Atrial fibrosis, an adaptive response to various insults, is mediated by excessive fibroblast proliferation resulting in the deposition of proteins within the cardiac interstitial space. Surgical biopsy and autopsy specimens from patients with AF have shown increased diffuse atrial fibrosis compared to those in sinus rhythm.[6–8] Innovative studies of late gadolinium enhancement on cardiac magnetic resonance (LGE-CMR) have revealed the presence of focal/cohesive LA fibrosis before and after ablation procedures.[5,9] However, the presence of global/diffuse LA fibrosis has not been noninvasively examined.

Cardiac magnetic resonance (CMR) T1 mapping is a recently introduced technique to quantify contrast-enhanced T1 relaxation time in tissues of interest. It has been shown that an inverse linear relationship exists between contrast-enhanced left ventricular (LV) myocardial T1 time and the burden of global myocardial fibrosis.[10,11] LV T1 mapping has been used to identify reduced T1 times as a surrogate of increased fibrosis in patients with acute and chronic myocardial infarction,[12] valvular disease,[13] heart failure,[10] nonischemic dilated cardiomyopathy,[14] and hypertrophic cardiomyopathy.[15] However, left atrial (LA) T1 mapping has not been investigated as a potential noninvasive measure of diffuse atrial fibrosis. The purpose of the present study

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was to (a) establish the feasibility of LA T1 measurements, (b) determine the range of LA T1 values in patients with AF vs healthy volunteers, and (c) validate T1 mapping vs global LA intracardiac electrogram amplitude measures as a surrogate of diffuse atrial fibrosis.

Methods

Patients with AF

The study protocol was reviewed and approved by the Johns Hopkins Institutional Review Board. We recruited patients referred for pulmonary vein antral isolation (PVAI) for the treatment of symptomatic AF from January 2011 to April 2012. During the course of the study, CMR was performed in 57 patients before AF ablation. We excluded 6 patients with AF from this study because of respiratory motion artifacts on CMR images. Therefore, data from 51 patients (74% man; median age 55 [interquartile range (IQR) 51–65] years) were acquired and analyzed. The baseline AF type was categorized as paroxysmal (AF self-termination within 7 days), persistent (AF lasting >7 days or requiring cardioversion), or long-standing persistent (AF lasting >1 year). In addition, patients were defined as having lone AF if they were $\leq$60 years in age and free of hypertension, diabetes mellitus, coronary artery disease, and cardiomyopathy.

Healthy volunteers

Seventeen healthy volunteers underwent CMR scans including the T1 mapping sequence. One volunteer was excluded from analysis owing to respiratory motion artifacts, and the remaining 16 healthy volunteers (31% man, median age 26 [IQR 23–30] years) comprised the control group. The volunteers did not undergo invasive electroanatomic mapping.

T1 mapping protocol

All participants underwent CMR by using a 1.5 Tesla Avanto scanner (Siemens, Erlangen, Germany) and a 6-channel body matrix coil combined with an integrated 6-channel spine matrix for a total of 12 channels. To optimize ablation success,[16] patients with persistent or long-standing persistent AF were started on antiarrhythmic medications and referred for external cardioversion 3–4 weeks before CMR and AF ablation. Of 51 patients with AF included in this study, 8 were in AF at the time of CMR and the remaining patients with AF and healthy volunteers (88% of total participants) were in sinus rhythm. The CMR examination was performed by using the same methodology regardless of the presenting rhythm. The CMR examination was performed with the patient in the supine position, during expiratory apnea, and using electrocardiographic gating. Intravenous infusion of gadolinium contrast (Magnevist, Bayer Healthcare Pharmaceuticals, Montville, NJ, 0.15–0.20 mmol/kg) was done at an injection rate of 2 mL/s, followed by a 20–30-mL saline flush. A vertical long-axis modified Look-Locker inversion-recovery sequence (11 images within 17 heartbeats, slice thickness 6 mm, repetition time 200–250 ms, echo time 1.08 ms, flip angle 35º, matrix 192 $\times$ 154, field of view 30–36 $\times$ 32–36 cm) was performed after contrast injection (median delay 23.8 [IQR 20.9–31.0] minutes).

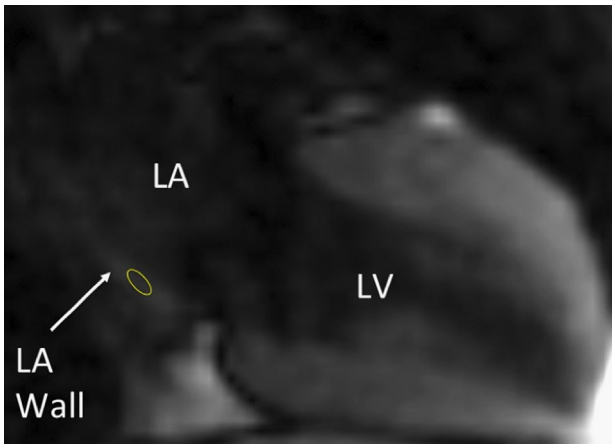

Figure 1 Methodology for the measurement of left atrial T1 relaxation time. The cardiac magnetic resonance image was acquired by using a vertical long-axis modified Look-Locker inversion-recovery sequence. The region of interest (yellow circle) has been placed on the posterior LA wall. LA = left atrial; LV = left ventricular.

Analysis of T1 relaxation times

A single reader who was blinded to participants' case vs control status and clinical information performed T1 mapping. All images were processed off-line by using MASS research software (V2010-EXP, Leiden University, Leiden, The Netherlands), as previously described.[17] Regions of interest (ROIs) were placed on the LA posterior wall myocardium for all phases in the Look-Locker sequence (Figure 1). The pixel-by-pixel fit was performed to a 3-parameter model ($A - B \exp[-TI/T1^*]$) to obtain myocardial T1 as $T1 = (B/A - 1)T1^*$. Only pixels where the χ^2 test for goodness of fit was significant with the level of significance $\alpha = 0.05$ were included in the average myocardial T1 value.[18] Mean T1 times were normalized to a standard gadolinium dose (0.15 mmol/kg), delay times between contrast administration and LL sequence acquisition (11 minutes), and glomerular filtration rate (90 mL/min/1.73 m^2) by using the multicompartment model previously validated by Gai et al.[17] Similarly, T1 measurements were performed for the LV myocardium by using an ROI in the inferobasal portion of the inferoposterior wall. To assess the potential effects of intraobserver variability in the measurement of T1 relaxation times, we randomly selected a subset of 10 patients in whom the primary user repeated T1 measurements in a separate session. Similarly, to assess the potential effects of interobserver variability, we randomly selected 10 patients in whom a second reader repeated T1 measurements independently.

Electroanatomic voltage maps

At the beginning of each PVAI procedure, a detailed intracardiac point-by-point sampled LA voltage map was obtained by using the CARTO electroanatomic mapping