JACC: CARDIOVASCULAR IMAGING
VOL. 9, NO. 2, 2016

ISSN 1936-878X/$36.00
PUBLISHED BY ELSEVIER
http://dx.doi.org/10.1016/j.jcmg.2015.10.015

Left Atrial LGE and Arrhythmia Recurrence Following Pulmonary Vein Isolation for Paroxysmal and Persistent AF

Irfan M. Khurram, MD,[a] Mohammadali Habibi, MD,[a] Esra Gucuk Ipek, MD,[a] Jonathan Chrispin, MD,[a] Eunice Yang, MD,[a] Kotaro Fukumoto, MD,[a] Jane Dewire, BA,[a] David D. Spragg, MD,[a] Joseph E. Marine, MD,[a] Ronald D. Berger, MD, PhD,[a,b] Hiroshi Ashikaga, MD, PhD,[a,b] Jack Rickard, MD, MPH,[a] Yiyi Zhang, PhD,[c] Vadim Zipunnikov, PhD,[d] Stefan L. Zimmerman, MD,[e] Hugh Calkins, MD,[a] Saman Nazarian, MD, PhD[a,c]

ABSTRACT

OBJECTIVES The aims of this study were to: 1) use a novel method of late gadolinium enhancement (LGE) quantification that uses normalized intensity measures to confirm the association between LGE extent and atrial fibrillation (AF) recurrence following ablation; and 2) examine the presence of interaction and effect modification between LGE and AF persistence.

BACKGROUND Recurrent AF after catheter ablation has been reported to associate with the baseline extent of left atrial LGE on cardiac magnetic resonance. Traditional methods for measurement of intensity lack an objective threshold for quantification and interpatient comparisons of LGE.

METHODS The cohort included 165 participants (mean age 60.0 ± 10.2 years, 77% men, 57% with persistent AF) who underwent initial AF ablation. The association of baseline LGE extent with AF recurrence was examined using multivariable Cox proportional hazards models. Multiplicative and additive interactions between AF type and LGE extent were examined.

RESULTS During 10.2 ± 5.7 months of follow-up, 63 patients (38.2%) experienced AF recurrence. Baseline LGE extent was independently associated with AF recurrence after adjusting for confounders (hazard ratio: 1.5 per 10% increased LGE; $p < 0.001$). The hazard ratio for AF recurrence progressively increased as a function of LGE. The magnitude of association between LGE >35% and AF recurrence was greater among patients with persistent AF (hazard ratio: 6.5 [$p = 0.001$] vs. 3.6 [$p = 0.001$]); however, there was no evidence for statistical interaction.

CONCLUSIONS Regardless of AF persistence at baseline, participants with LGE ≤35% have favorable outcomes, whereas those with LGE >35% have a higher rate of AF recurrence in the first year after ablation. These findings suggest a role for: 1) patient selection for AF ablation using LGE extent; and 2) substrate modification in addition to pulmonary vein isolation in patients with LGE extent exceeding 35% of left atrial myocardium. (J Am Coll Cardiol Img 2016;9:142–8)

From the [a]Division of Cardiology, Johns Hopkins University, Baltimore, Maryland; [b]Department of Biomedical Engineering, Johns Hopkins University, Baltimore, Maryland; [c]Department of Epidemiology, Johns Hopkins University, Baltimore, Maryland; [d]Department of Biostatistics, Johns Hopkins University, Baltimore, Maryland; and the [e]Department of Radiology, Johns Hopkins University, Baltimore, Maryland. This study was funded by National Institutes of Health grants K23HL089333 and R01HL116280 and a Biosense Webster grant to Dr. Nazarian, the Dr. Francis P. Chiaramonte Foundation, The Norbert and Louise Grunwald Cardiac Arrhythmia Fund, the Marv Weiner Cardiac Arrhythmia Fund, and the Marilyn and Christian Poindexter Research Fund. Dr. Rickard is a consultant to Medtronic; and has served as a speaker for St. Jude Medical. Dr. Calkins is a consultant to Medtronic and St. Jude Medical; and has received research support from St. Jude Medical. Dr. Nazarian is a scientific advisor to Medtronic, CardioSolv, and Biosense Webster; and principal investigator for research funding to Johns Hopkins University from Biosense Webster. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received May 27, 2015; revised manuscript received September 16, 2015, accepted October 8, 2015.

Atrial fibrillation (AF) is associated with increased risk for mortality, heart failure, and thromboembolic events and has a worldwide prevalence of >33.5 million (1-3). Catheter ablation of AF is evolving as an effective therapy for symptomatic AF (4). Recurrent AF after ablation, however, remains a problem and has been reported to associate with the baseline extent of left atrial (LA) late gadolinium enhancement (LGE) on cardiac magnetic resonance (CMR) (5). Mechanistically, persistent AF appears to be more reliant on fibroblast proliferation and myocyte-fibroblast coupling than paroxysmal AF, which is dependent primarily on pulmonary vein triggers (6-8). Therefore, we sought to: 1) confirm the association of LA LGE with recurrent AF following ablation; and 2) examine the presence of interaction and/or effect modification between LGE and AF persistence prior to ablation.

SEE PAGE 149

ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation
CI = confidence interval
CMR = cardiac magnetic resonance
HR = hazard ratio
IIR = image intensity ratio
LA = left atrial
LGE = late gadolinium enhancement
PVI = pulmonary vein isolation

METHODS

PATIENT CHARACTERISTICS. The Johns Hopkins Institutional Review Board approved the study, and all patients provided written informed consent. Between November 2011 and December 2013, 171 consecutive patients with drug-refractory AF who were referred for initial catheter ablation procedures, were scheduled for a pre-procedural CMR, and consented to participate were prospectively enrolled.

CMR. All subjects underwent pre-procedural CMR as previously described (9-11). Images were acquired using a 1.5-T CMR scanner (Avanto, Siemens, Erlangen, Germany) with a phased-array cardiac coil. Pulse oximetry, blood pressure, and electrocardiographic monitoring were maintained during the CMR examination. Contrast-enhanced 3-dimensional fast low-angle shot magnetic resonance angiographic images were used to define LA and pulmonary vein anatomy. LGE CMR scans were acquired approximately 20 min after 0.2 mmol/kg gadolinium injection (gadopentetate dimeglumine, Bayer Healthcare Pharmaceuticals, Montville, New Jersey). The LGE sequence was a 3-dimensional inversion recovery prepared respiratory triggered and navigated, electrocardiographically gated, and fat-suppressed fast spoiled gradient echo sequence (repetition time 2.5 to 5.5 ms, echo time 1.52 ms, field of view 340 mm, flip angle 10°, inversion time 240 to 300 ms, 1.3 × 1.3 mm in-plane spatial resolution, 2-mm slice thickness).

LA LGE EXTENT QUANTIFICATION. The LGE CMR images were processed using QMass MR software version 7.2 (Leiden University Medical Center, Leiden, the Netherlands). The LA myocardium was defined by manual placement of epicardial and endocardial contours by observers who were masked to clinical data (approximately 30 min of analysis time per image set). The image intensity ratio (IIR), a previously described (10,11) LGE CMR analysis technique that normalizes the myocardial image intensity by blood pool intensity, was used. The extent of LA LGE was quantified using the 0.97 image intensity threshold previously validated against LA bipolar voltage <0.5 mV (11). For this study, we used a threshold of <0.5 mV given prior use of this threshold to demarcate abnormal LA myocardium (12). LA volume measurements included the LA appendage as well as pulmonary vein antra and were limited anteriorly to the mitral valve plane.

CATHETER ABLATION. All patients underwent wide-area circumferential pulmonary vein isolation (PVI) as previously described (10,11). Briefly, a double transatrial septal puncture was performed under fluoroscopic guidance. An endocardial map of the left atrium was created with an electroanatomic mapping system (CARTO, Biosense Webster, Diamond Bar, California) and superimposed on the pre-existing CMR image of the chamber. With routine hemodynamic and electrocardiographic monitoring, a 4-mm-tipped irrigated ablation catheter (Thermocool, Biosense Webster) was advanced under fluoroscopic guidance to the left atrium. Circumferential lesions were applied surrounding the pulmonary veins. Additional ostial lesions were targeted to remaining pulmonary vein potentials using a circular multipolar electrode-mapping catheter (Lasso, Biosense Webster). Entrance block into the pulmonary veins was confirmed in all patients as the primary procedural endpoint. Additionally, when possible by demonstration of pulmonary vein capture, exit block was documented. To prevent short-term recurrences of AF, previously ineffective antiarrhythmic medications were continued for at least 3 months.

CLINICAL FOLLOW-UP. Recurrent AF was defined on the basis of the 2012 Heart Rhythm Society consensus document as symptomatic or asymptomatic AF, atrial tachycardia, or atrial flutter of >30 seconds in duration after a 3-month blanking period (4). Close communication via clinic visits and phone was maintained with all patients following the ablation. If symptoms suggestive of an arrhythmia occurred, patients were asked to undergo 24-h Holter monitoring or 30-day event monitoring depending on symptom frequency. In the absence of reported symptoms, patients were evaluated for recurrence at 6 and 12 months.