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Resting and Exercise-Induced Left Atrial Hypertension in Patients With Atrial Fibrillation

The Causes and Implications for Catheter Ablation

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ABSTRACT

OBJECTIVES The aim of this paper was to investigate the prevalence of resting and exercise-induced left atrial hypertension (LAH) in patients with nonvalvular atrial fibrillation (AF), association of the LAH with other cardiac abnormalities, and its implications for AF catheter ablation.

BACKGROUND The clinical role of LAH in patients with established AF is largely unknown.

METHODS Patients scheduled for catheter ablation of AF (n = 240, age 60 ± 10 years, 67% men, 62% paroxysmal AF) underwent detailed echocardiography, assessment of quality of life (QoL), left atrial (LA) voltage mapping, and measurement of the LA pressure at rest and during isometric handgrip exercise. After ablation they were followed for AF recurrence for 16 ± 6 months.

RESULTS Resting and exercise-induced LAH (mean LA pressure >15 mm Hg) occurred in 15% and 34% of the patients, respectively. Both the patients with resting and exercise-induced LAH had typical features of latent heart failure with preserved ejection fraction associated with advanced LA structural and functional remodeling. AF recurred after ablation in 45% of the patients. LAH was an independent risk factor for arrhythmia recurrence (hazard ratio 1.7, 95% confidence interval 1.2 to 2.2). The patients with LAH had worse baseline QoL, but they benefited significantly more from a successful ablation than the patients without LAH.

CONCLUSIONS Presence of either resting or exercise-induced LAH identified AF patients with a distinct clinical profile, extensive LA substrate, and different clinical response to catheter ablation. Stratification of AF patients based on the LA exercise hemodynamics could help in the future to tailor the ablation strategy. (J Am Coll Cardiol EP 2017;■:■–■)

Catheter ablation has become a standard therapy for atrial fibrillation (AF) (1). However, to be effective, the ablation strategy must reflect the patient-specific left atrial (LA) pathology. Patients with less diseased LA may benefit from a simple isolation of the pulmonary veins, whereas patients with more diseased LA may have a better outcome after extensive substrate-targeting ablation (2).

Whether a patient has diseased LA is currently estimated based on the AF duration, presence of comorbidities, cardiac imaging, or LA voltage mapping. This approach is inaccurate and reflects only a few aspects of the LA disease (1). Direct assessment of the LA pressure could provide a more complex and self-contained information on the LA condition. It is based on the key role of LA hypertension (LAH) in the

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ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation

HFpEF = heart failure with preserved ejection

LA = left atrium/atrial

LAH = left atrial hypertension

LV = left ventricle/ventricular

QoL = quality of life

SR = sinus rhythm

LA remodeling, where it acts as a unifying pathway and a major force through which diverse clinical factors realize their detrimental effects (3). Assessment of the LA pressure during an exercise stress test could even more realistically reflect the LA hemodynamics and it could uncover conditions that do not manifest at rest.

In this study we hypothesized that the presence of either resting or exercise-induced LAH in patients with nonvalvular AF and preserved left ventricular (LV) ejection fraction would identify a distinct subgroup of patients who would have more diseased LA, different clinical responses to AF ablation, and who could benefit from a different strategy of the ablation. We also investigated factors causing LAH and its association with other cardiac abnormalities.

METHODS

STUDY PROTOCOL. The study enrolled 240 patients who underwent catheter ablation for AF at our institution. Excluded were patients with a cardiomyopathy, congenital heart disease, valvular heart disease, or LV ejection fraction <40%. The study was approved by institutional ethical committee and all patients provided written consent with the investigation.

On the day before ablation, patients underwent clinical evaluation, echocardiography, blood sampling for analysis of cardiac biomarkers, and assessment of quality of life (QoL) by the short form 36-item (SF-36) questionnaire. Catheter ablation was performed under conscious sedation using 3-dimensional navigation (CARTO, Biosense Webster, Diamond Bar, California) and point-by-point radiofrequency ablation (3.5-mm Navistar Thermocool catheter, Biosense Webster). All patients underwent circumferential pulmonary vein isolation. Additional LA linear lesions (n = 83), coronary sinus ablations (n = 42), and electrogram-guided ablations (n = 33) were performed stepwise if the AF sustained and the LA mapping revealed low-voltage areas or complex fractionated atrial electrograms. The LA pressure was not considered while planning the ablation strategy.

After ablation, the patients were followed during regular visits for a minimum of 1 year. The details of our follow-up examinations of patients after AF ablation have been described elsewhere (4). The involved physicians were blinded to the baseline study data. Antiarrhythmic drugs were discontinued in 86% of the patients within the first 3 months after the ablation. Arrhythmia recurrence was defined as any documented symptomatic or asymptomatic episode of AF or atrial tachycardia lasting >30 s, after excluding a blanking period of 3 months (5). QoL was re-assessed at 6 months after ablation.

ASSESSMENTS OF CARDIAC STRUCTURE AND FUNCTION. Echocardiography (Vivid 7, GE Healthcare, Chalfont St Giles, United Kingdom) was performed by experienced operators according to the guidelines (6,7). LA phasic function, wall stress, and diastolic stiffness were estimated as previously described (8). The phasic LA volumes and maximal right atrial volume were obtained by the area-length method in the apical 4-chamber view. Right atrial pressure was estimated based on the inferior vena cava diameter and collapsibility (7). Systolic pulmonary artery pressure was determined from the right atrial pressure and tricuspid regurgitant jet peak velocity. In case of present AF, all measurements were obtained by averaging of at least 5 consecutive beats.

LA tissue pathology was assessed by endocardial bipolar voltage mapping during spontaneous rhythm, using the ablation catheter. Adequate catheter contact was verified real-time by checking the appearance of the atrial electrograms, intracardiac echocardiography, and tactile feedback. The voltage maps (>100 points in 94% of the patients) were carefully edited, contiguous regions with low voltage were manually delineated, and the surface area of the low-voltage regions was related the total LA surface area (9). For definition of the low voltage we used 3 different cut-offs: <0.5 mV, <0.15 mV, and a combined cut-off of <0.5 mV for patients in sinus rhythm (SR) and <0.15 mV for patients in AF.

LA loading was estimated by midregional pro-atrial natriuretic peptide (MR-proANP assay, BRAHMS, Henningsdorf, Germany), LV loading was assessed by B-type natriuretic peptide (BNP), and galectin-3 served as a biomarker of fibrosis (BNP and Galectin-3 Architect assays, Abbott Diagnostics, Lake Forrest, Illinois).

MEASUREMENT OF LA PRESSURE. LA pressure was measured at the beginning of the ablation procedure through an 8 F transseptal sheath placed in the LA cavity. The pressure transducer was zeroed at the midthoracic level. LA pressure, heart rate, and right-arm blood pressure were recorded at rest and subsequently during 3 min of isometric handgrip exercise. The handgrip was performed with a constant force of 40% of maximum voluntary contraction using a dynamometer (Kern & Sohn, Balingen, Germany) placed in the patient's left hand (10). The patients were encouraged to breathe regularly to avoid Valsalva maneuver. LA mean pressure was calculated over several breath cycles. LAH was defined as the LA