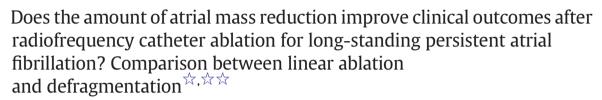
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Seong Woo Han <sup>a,1</sup>, Seung Yong Shin <sup>b,1</sup>, Sung Il Im <sup>c</sup>, Jin Oh Na <sup>c</sup>, Cheol Ung Choi <sup>c</sup>, Seong Hwan Kim <sup>c</sup>, Jin Won Kim <sup>c</sup>, Eung Ju Kim <sup>c</sup>, Seung-Woon Rha <sup>c</sup>, Chang Gyu Park <sup>c</sup>, Hong Seog Seo <sup>c</sup>, Dong Joo Oh <sup>c</sup>, Chun Hwang <sup>d</sup>, Hong Euy Lim <sup>c,\*</sup>

- a Department of Cardiology, Hallym University Hangang Sacred Heart Hospital, 94-200 Yeongdeungpo-dong 2-ga, Yeongdeungpo-gu, Seoul, Republic of Korea
- b Division of Cardiology, Heart Research Institute, College of Medicine, Chung-Ang University, 224-1 Heukseok-dong, Dongjak-gu, Seoul, Republic of Korea
- <sup>c</sup> Division of Cardiology, Cardiovascular Center, Korea University Guro Hospital, Korea University College of Medicine, 148, Gurodong-ro, Guro-gu, Seoul, Republic of Korea
- <sup>d</sup> Division of Cardiology, Utah Valley Regional Medical Center, 1055 North 500 West, Provo, UT 84604, USA

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#### ABSTRACT

Background: Although a large isolated surface area of the left atrium (LA) may improve the success rate of catheter ablation (CA) for paroxysmal atrial fibrillation (AF), little is known about the relation between clinical outcomes and the amount of atrial mass reduction (AMR: ratio of total isolated and ablated areas to LA surface area) in different ablation strategies for patients with long-standing persistent AF (L-PeAF).

Methods: We randomly assigned 119 consecutive L-PeAF patients to adjunctive linear ablation (n=60) or complex fractionated atrial electrogram (CFAE)-guided ablation (n=59) after circumferential antral pulmonary vein isolation (PVI). Linear lesions included roof and anterior lines with conduction block. LA defragmentation was performed with an automated CFAE-detection algorithm. Cavotricuspid isthmus block was performed in all patients. Creatine kinase-MB (CK-MB) and troponin-T levels were measured 1 day post-CA.

Results: CK-MB and troponin-T levels were higher, ablation time was longer, and AMR was greater in the CFAE-guided ablation group than in the linear ablation group. AF termination during CA was more frequently observed in the linear ablation group than in the CFAE-guided ablation group (P=0.031). Twelve months after a single procedure, recurrence occurred in 16 (26.7%) patients with linear ablation and 27 (45.8%) patients with CFAE-guided ablation (P=0.023). On multivariate analysis, LA volume and ablation method were the only independent risk factors for arrhythmia recurrence.

Conclusion: Conduction block through linear lines + PVI was an efficient ablation strategy for L-PeAF, whereas the AMR amount did not influence clinical outcomes.

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#### 1. Introduction

Pulmonary vein isolation (PVI) is currently the standard therapy for selected patient groups and has been considered a first-line therapy for those with symptomatic paroxysmal atrial fibrillation (AF) [1].

E-mail addresses: hongeuy@korea.ac.kr, h3lim@medimail.co.kr (H.E. Lim).

However, PVI alone is not sufficient to eliminate arrhythmogenic substrates in patients with long-standing persistent AF (L-PeAF) [2]. Although several investigators have suggested that additional linear lesions or defragmentation of complex fractionated atrial electrograms (CFAE) in the left atrium (LA) may improve clinical outcomes after catheter ablation (CA) for L-PeAF [3,4], the limited clinical efficacy has led to a search for the ideal CA strategy.

Because experimental and clinical evidence has revealed that a critical mass of atrial tissue is necessary to maintain AF [5], suggesting that the efficacy of AF ablation may be related to the extent of the ablated tissue, there has been a trend toward ablation of extensive lesions performed in a stepwise manner [6]. However, more extensive ablation may not only increase the risk of complications [7] but may also be associated with arrhythmia recurrence through the creation of proarrhythmic substrates caused by iatrogenic myocardial injury [8,9].

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<sup>\*</sup> Corresponding author at: Cardiovascular Center, Division of Cardiology, Department of Internal Medicine, Korea University Guro Hospital, Korea University College of Medicine, 97, Guro-dong, Guro-gu, Seoul 152-703, Republic of Korea. Tel.:  $+82\ 2\ 2626\ 1046$ ; fax:  $+82\ 2\ 867\ 9093$ .

<sup>&</sup>lt;sup>1</sup> The first 2 authors equally contributed to this study.

To improve success rates, various adjunctive atrial modifications, targeting both AF triggers and the perpetuating substrate, have been incorporated into CA for L-PeAF [3,4]. However, little is known about the relation between clinical outcomes and the amount of atrial mass reduction (AMR) in different ablation strategies for L-PeAF patients.

The aims of this study were to identify whether the degree of AMR influences long-term clinical outcomes after a single procedure, and to determine which of the 2 ablation strategies was more effective in patients who underwent CA for L-PeAF.

#### 2. Methods

#### 2.1. Study population

From December 2008 to August 2011, we prospectively enrolled 119 consecutive L-PeAF patients who underwent CA. L-PeAF was defined according to the most recent guidelines of the Heart Rhythm Society and the European Cardiac Arrhythmia Society [10]. Exclusion criteria were the presence of visible LA thrombi on transesophageal echocardiography (TEE), previous AF ablation or cardiac surgery, cardiomyopathy, more than mild valvular disease, congenital heart disease, aortic aneurysm or dissection, an acute cerebrovascular event within the preceding 3 months, hyperthyroidism, and any acute or chronic inflammatory diseases. All antiarrhythmic drugs were discontinued at least 5 half-lives before the examination. Amiodarone was discontinued at least 8 weeks earlier. All patients were on continuous anticoagulation therapy with a target international normalized ratio of 2–3. Each participant signed an informed consent form before the study, which was approved by the Human Subjects Review Committee of Korea University Guro Hospital.

The authors of this manuscript certify that they comply with the Principles of Ethical Publishing in the *International Journal of Cardiology*.

#### 2.2. Transthoracic echocardiography

All examinations were performed using a commercially available Vivid  $7^{TM}$  (GE Medical Systems, Vingmed, Horten, Norway) ultrasound system. All recorded echocardiograms were collected and analyzed using an offline computer analysis station (Echopac<sup>TM</sup> 6.3.4; GE Medical Systems).

All measurements were taken from 3 consecutive cardiac cycles and averaged. The maximal LA volume (LAV) was measured manually using the modified Simpson's method, by tracing the endocardial border in the apical 4- and 2-chamber views over the cardiac cycle after zooming in on the LA. Each echocardiographic parameter was determined according to the recommendations of the American Society of Echocardiography [11].

#### 2.3. Ablation procedure

Before CA, TEE and multi-slice computerized tomography (MSCT) were performed in all patients. Intracardiac electrocardiograms (ECGs) were recorded using a PruckaCardioLab<sup>TM</sup> electrophysiology system (General Electric Health Care Systems Inc., Milwaukee, WI, USA), and a 3-dimensional (3D) electroanatomical mapping system (NavX; St. Jude Medical Inc., Minnetonka, MN, USA) was used in all patients. After double transseptal puncture, systemic anticoagulation was achieved with intravenous heparin to maintain an activated clotting time between 300 and 350 s. After the 3D geometry of the LA and pulmonary veins (PVs) had been determined using the NavX mapping system and merged with the volumerendered MSCT image, all PVs were mapped with a decapolar circular catheter (Lasso; Biosense Webster, Diamond Bar, CA, USA). An open-irrigation, 3.5-mm-tip deflectable catheter (Celsius; Biosense Webster) was used for mapping and ablation. Radiofrequency energy was delivered as follows: maximum power output, 25–30 W; flow rate, 17–30 mL/min; and maximum temperature, 48 °C. The endpoint for each individual application at a given site was either total voltage abatement or current application of up to 40 s with adequate tissue contact and power delivery.

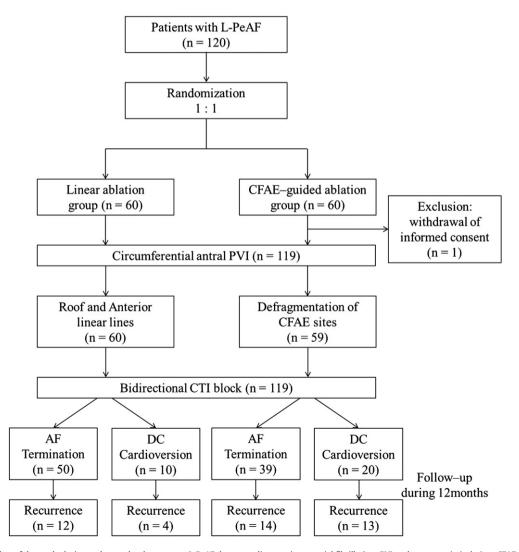


Fig. 1. Schematic algorithm of the study design and procedural outcomes. L-PeAF: long-standing persistent atrial fibrillation; PVI: pulmonary vein isolation; CFAE: complex fractionated atrial electrograms; CTI: cavotricuspid isthmus; AF: atrial fibrillation.

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