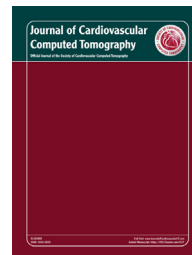




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## Original Research Article

# Periatrial epicardial adipose tissue thickness is an independent predictor of atrial fibrillation recurrence after cryoballoon-based pulmonary vein isolation



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## ABSTRACT

**Background:** Epicardial adipose tissue (EAT) is a metabolically active fat depot. Studies have investigated the effect of EAT thickness on outcomes of radiofrequency catheter ablation of atrial fibrillation (AF). However, data on the relationship between EAT thickness and outcome of cryoballoon-based pulmonary vein isolation (PVI) are lacking.

**Objective:** In this study, we investigate the association between EAT thickness and AF recurrence after cryoballoon-based PVI.

**Methods:** Patients with symptomatic paroxysmal or persistent AF despite  $\geq 1$  antiarrhythmic drug(s) were scheduled for cryoballoon-based PVI for AF per the recent recommendations. Periatrial, periventricular, and total EAT thickness measurements were obtained from preprocedural multidetector CT scans.

**Results:** A total of 249 patients ( $55.6 \pm 10.7$  years; 48.2% male; 18.5% persistent AF) were involved in the study. Patients were followed-up for 29 months (8–48 months). When blanking period was considered, freedom from AF after the ablation procedure was 75.9% at a median follow-up of 29 months. Total periatrial EAT thickness ( $18.1 \pm 6.2$  vs  $14.7 \pm 4.7$  mm;  $P < .001$ ) was greater in patients with late AF recurrence when compared to those without. On the other hand, periventricular or total EAT thickness measurements did not differ between both groups ( $P > .05$ ). Multivariate Cox proportional hazard regression analysis showed that periatrial EAT thickness (hazard ratio, 1.086;  $P = .001$ ) and left atrial volume index (hazard ratio, 1.144;  $P < .001$ ) were independent predictors for late AF recurrence.

**Conflict of interest:** The authors report no conflicts of interest.

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**Conclusion:** Quantification of EAT thickness from preprocedural multidetector CT scans may serve as a beneficial parameter for prediction of AF recurrence after cryoballoon-based PVI.

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## 1. Introduction

Epicardial adipose tissue (EAT) is the adipose tissue located between the outer wall of the myocardium and the visceral pericardium. Its proximity to cardiac structures (ie, vessels, myocardium) and its shared blood supply with the cardiac microcirculation makes it a unique fat depot.<sup>1</sup> EAT is a metabolically active organ that generates various bioactive molecules that are directly involved in inflammation and is known to modulate vascular and myocardial functions including adiponectin, tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), interleukin 6 (IL-6), and monocyte chemoattractant protein-1 (MCP-1).<sup>2,3</sup> Its paracrine effects on many types of cardiovascular disease, including metabolic syndrome,<sup>4</sup> coronary artery disease<sup>5,6</sup> and atrial fibrillation, have aroused interest. Cardiac CT offers accurate quantification and assessment of distribution for EAT.

Several studies have investigated the relationship between the EAT thickness and presence of AF.<sup>7,8</sup> Its association between AF recurrence after radiofrequency catheter ablation (RFCA) for AF has also been reported, and inflammation leading to left atrial (LA) remodeling has been proposed to be the underlying link.<sup>9–11</sup> However, the relationship between EAT thickness and AF recurrence in patients undergoing cryoballoon-based pulmonary vein isolation (PVI) for AF has not been thoroughly evaluated yet. In this study, we aimed to investigate this association.

## 2. Materials and methods

### 2.1. Study population

During the period between September 2010 and February 2014, 249 patients with symptomatic paroxysmal or persistent AF despite  $\geq 1$  antiarrhythmic drug(s) who were scheduled for cryoballoon-based AF ablation procedure per the recent consensus recommendations were included in this retrospective study.<sup>12</sup>

Atrial fibrillation episodes that either lasted  $>7$  days or required termination by cardioversion, either with drugs or with direct current cardioversion, were defined as persistent, where AF episodes self-terminating within 7 days were defined as paroxysmal AF.<sup>13</sup> Patients who had moderate to severe valvular disease, thrombus in LA, abnormal thyroid function, contraindication to anticoagulation, and left ventricular ejection fraction  $< 50\%$  were excluded from the study.

Baseline demographic and clinical characteristics, including age, sex, body mass index, hypertension, diabetes mellitus, coronary artery disease, smoking history, and alcohol consumption, were recorded for all patients. Data related to the diagnosis of AF including date of first diagnosis,

symptomatic severity based on European Heart Rhythm Association score,<sup>14</sup> and antiarrhythmic medications were also recorded. The study was in compliance with the principles outlined in the Declaration of Helsinki and approved by the institutional ethics committee.

### 2.2. Preprocedural management

All patients underwent transthoracic echocardiography (TTE) within 1 week before ablation to assess intracavitary dimensions, left ventricular ejection fraction, and to exclude valvular heart disease. LA area and LA length were measured in the apical 4-chamber and apical 2-chamber views. LA volume was derived using the biplane area-length method. LA volume index (LAVI) was calculated based on the patient's body surface area.<sup>15</sup> Transoesophageal echocardiography was performed to rule out the presence of thrombus in the LA appendage the day before procedure. Furthermore, patients underwent a preprocedural multidetector CT scan with 3-dimensional construction of the LA to assess detailed LA anatomy, including evaluation of the pulmonary vein (PV) configuration. Anticoagulation was discontinued at least 48 to 72 hours before the procedure and the preprocedural interval was bridged with enoxaparin 1 mg/kg. Treatment with antiarrhythmic drugs was discontinued for at least 3 days before the procedure.

### 2.3. Epicardial fat tissue thickness measurement

CT scans were performed using dual-source 64-slice multidetector CT scanner (SOMATOM Definition; Siemens, Erlangen, Germany). Sublingual nitrate (5 mg of isosorbide dinitrate; Fako Isordil) was administered 2 to 4 minutes before image acquisition to dilate the coronary arteries. The coronary angiographic scan was obtained with an injection of 80 mL of nonionic contrast medium (350 mg I/mL iomeprol; Bracco Omnipaque) at a flow rate of 6 mL/s followed by 50 mL of saline solution, and contrast administration was controlled with bolus tracking. The scan parameters were detector collimation of  $2 \times 32 \times 0.6$  mm, slice acquisition of  $64 \times 0.6$  mm, gantry rotation time of 330 ms, temporal resolution of 83 ms, pitch of 0.20 to 0.47 adapted to the heart rate, tube current of 390 mAs per rotation, and tube potential of 120 kV. Scanning time was approximately 5.7 to 8.4 seconds, depending on the cardiac dimensions and pitch and breathholding was used to minimize motion artifact. Prospective electrocardiography (ECG) tube current modulation (ECG pulsing) for radiation dose reduction was used for all patients. Retrospective gating technique was used to synchronize data reconstruction with the ECG signal. The reconstructions were made in all cardiac phases at 50-ms intervals at a slice thickness of 0.75 mm and a reconstruction increment of 0.5 mm. The reconstruction interval with the fewest motion artifacts was chosen and used for further

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