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Original

Right Atrial Volume Calculated by Multi-detector Computed Tomography: Useful Predictor of Atrial Fibrillation Recurrence after Pulmonary Vein Catheter Ablation

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Abstract: We investigated whether right atrial (RA) volume could be used to predict the recurrence of atrial fibrillation (AF) after pulmonary vein catheter ablation (CA). We evaluated 65 patients with paroxysmal AF (mean age, 60 + 10 years, 81.5% male) and normal volunteers (57 ± 14 years, 41.7% male). Sixty-four-slice multi-detector computed tomography was performed for left atrial (LA) and RA volume estimations before CA. The recurrence of AF was assessed for 6 months after the ablation. Both left and right atrial volumes were larger in the AF patients than the normal volunteers (LA: 99.7 + 33.2 ml vs. 59.7 + 17.4 ml; RA: 82.9 + 35.7 ml vs. 43.9 + 12 ml; P < 0.0001 for both). A total of 16 patients (24.6 %) showed recurrence of AF, involving both atrial volumes (LA: 125.8 + 36.9 ml in patients AF recurrence vs. 91.1 + 27.1 ml in 49 patients with no recurrence, P = 0.001; RA: 117.5 + 40.9 ml vs. 71.6 + 25.5 ml, P < 0.0001). The sensitivity with large LA volumes (>100 ml) for predicting the recurrence of AF was 81.3% in 13 of 16 patients with AF recurrence, and the specificity was 69.4% in 34 of 49 patients without recurrence. The sensitivity with large RA volumes (> 87 ml) was 81.3% in 13 of 16 patients with AF recurrence, and the specificity was 75.5% in 37 of 49 patients without recurrence. RA volume is a useful predictor of the recurrence of AF, similar to LA volume.

Key words: atrial fibrillation, catheter ablation, multi-detector computed tomography, atrial volume

Introduction

Atrial fibrillation (AF) is a common sustained arrhythmia encountered in clinical practice[1]. AF prevalence is increasing due to a combination of factors including an ageing population, the rising prevalence of chronic heart disease, and more frequent diagnosis through the use of ambulatory monitoring devices[2,3]. Radiofrequency percutaneous catheter

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ablation (CA) of AF with pulmonary vein isolation is currently the standard therapy for selected patients[4,5]. It is also considered as first-line therapy for symptomatic patients with paroxysmal AF, small left atrial (LA) dimensions, and no evidence of structural heart disease[4–6]. An enlarged LA volume is a known predictor of AF recurrence after CA in patients with AF[1,7]. Multidetector (MD) computed tomography (MDCT) allows multidimensional reconstruction of patient-specific cardiac anatomy[1,8]. CT-rendered volumes add a third dimension to an otherwise two-dimensional ablation procedure, allowing better delineation of the LA anatomy with precise volume estimation and increased electroanatomical mapping accuracy[9,10–12]. However, patients with AF also show increased right atrium (RA) volumes[13]. We therefore, we investigated whether measuring of RA volume is useful for predicting the recurrence of AF.

Methods

Study Population

This study enrolled patients with a history of palpitations and diagnosed with paroxysmal AF from April 2008 to November 2009 at Showa University Hospital. Arrhythmia was diagnosed on the basis of documented AF by ambulance monitoring, 12-lead electrocardiography (ECG), or Holter monitoring. A final diagnosis of AF was made when visible P wave were absent on all 12-leads of the ECG and an irregular random ventricular response was present. AF was considered paroxysmal if the fibrillatory process ended spontaneously after some seconds, minutes, hours, or up to 7 days[4]. Those patients with persistent (not self terminating, but recovery to sinus rhythm following therapy) or permanent AF were not enrolled in this study. Left ventricular ejection fraction (LVEF) was measured by two-dimensional echocardiography before the study and patients with LVEF $<$ 50%, history of valvular disease including of rheumatic cause, congenital heart disease, ischemic heart disease, or cardiomyopathy were also excluded. Patients were also excluded from this study if they had pre-excitation syndrome, atrioventricular tachycardia or ventricular tachyarrhythmia, atrial flutter, or a pacemaker implanted before the study. All patients underwent transesophageal echocardiography 24–72 hours before the procedure of pulmonary vein CA to exclude the presence of LA thrombus. Finally, 65 patients (mean $\pm$ standard deviation, age: 60$\pm$ 10 years, 81.5% males) with paroxysmal AF without structural heart disease and with preserved cardiac function were recruited for the final study cohort. Twelve normal healthy volunteers were also recruited as the control group (57 $\pm$ 14 years, 41.7% male). Sixty-four MDCT scanning was performed systematically up to 1 week before the procedure, for electroanatomical mapping integration[14], pulmonary vein anatomy delineation, and atrial volume estimations. Scanning was performed in a single breath hold in the cranio-caudal direction from aortic arch to diaphragm, being gated to the cardiac cycle through ECG synchronization. The pulmonary vein CA procedure was guided by CARTO merge electroanatomical mapping[14]. Three catheters were introduced via the right femoral vein under local anesthesia, supplemented by sedation when necessary. An irrigated-tip ablation catheter and a duodecapolar circular mapping catheter were placed at the pulmonary vein ostia via transeptal access. Irrigated-radiofrequency ablation was performed with continuous lesions encircling both pulmonary veins and deployed more than 5 mm from the pulmonary vein ostia[4]. Thus, the patients were submitted to complete isolation of all the pulmonary veins by a conventional procedure. Clinical success or recurrence of AF was assessed for 6 months, after the ablation, defined by the absence or presence, respectively, of symptomatic or documented AF by periodic electrocardiography and at least one 24-hour Holter monitoring after ablation. All patients gave written informed consent before this study, and the protocol was approved by our Institutional Review Board. Data collected prospectively included demographics, existing medical diagnoses, symptoms, risk factors for vascular disease, medications, previous cardiac procedures, and prior history of vascular event.

Scan Protocol and Data Acquisition of MDCT

All patients were scanned with a 64-slice scanner (SOMATOM Sensation 64 Cardiac, Siemens Medical Solutions, Forchheim, Germany). A bolus of contrast media (Omnipaque, 350 mg iodine / ml, Daiichi Pharmaceutical Co, Tokyo, Japan) was injected into an antecubital vein, followed by flushing with 20–50 ml of saline. The amount of contrast media used for the scan was determined according to the patient's body weight and scan time as follows: total dose = (scan time + 4 second) × 0.07 × body weight. The region of interest was placed within the ascending aorta and the scan was started when the CT density was 150 Hounsfield units higher than the baseline CT. The scan was performed between aortic arch and diaphragm with the following parameters: collimation width 64×0.6 mm; rotation time 330 ms; tube voltage 120 kV; effective tube current 800 mAs; table feed 11.5 mm / rotation, and pitch 0.2. Image reconstruction was retrospectively gated to an ECG, and ECG-gated datasets were reconstructed with a slice thickness of 0.75 mm and a interval of 0.7 mm at the point of 330 msec of the cardiac cycle before QRS complex[14, 15].

LA and RA volumes were measured using OsiriX software as an application for the MacOS X operating system (version 3.3.2)[16] (Fig. 1). Each short-axis CT image for the interval of 0.7 mm was picked up, and the region of interest was set up on the LA and RA areas. Thus, LA and RA volumes were quantitatively calculated from three-dimensional images using OsiriX software[17] (Fig. 2). Measurements were performed without knowledge of the clinical history. To assess interobserver variability, the LA volume measurements were repeated by a second reviewer blind to the findings of the first observer; there was an excellent correlation between those measurement sets ($P < 0.0001$).

Statistical Analysis

For descriptive purposes, the patients were divided into two groups on the basis of the predictors such as LA or RA volumes. Continuous variables were presented as means±

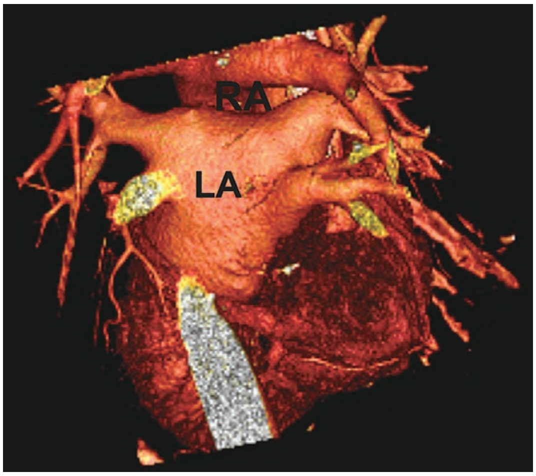

Fig. 1. Three-dimensional renderings of left atrium and pulmonary veins.

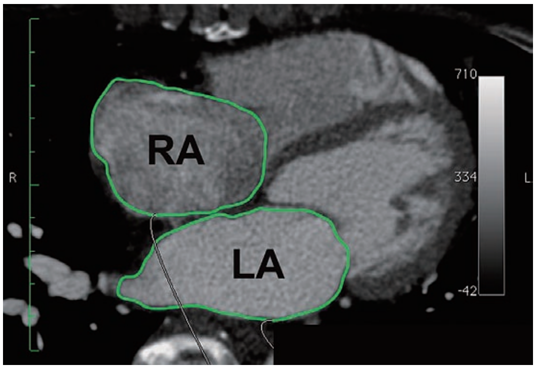

Fig. 2. The evaluation of left atrial (LA) and right atrial (RA) volumes. Semi-automatic software with atrium endocardial contour, automatic detection, and operator correction using OsiriX soft software.

standard deviation. Differences between groups (successful pulmonary vein ablation groups, AF recurrence group, and control group) were tested using ANOVA, the post-hoc test, the paired t-test, or the chi-square test, as appropriate. Receiver operating characteristic analysis was performed to define thresholds for those predictors; this analysis provided optimal sensitivity and specificity in predicting the recurrence of AF. The association between large atrial volume and recurrence of AF after CA was formally tested by construction of multivariate logistic regression analysis. The statistical analysis was done using SPSS for Windows version 11 (SPSS Inc, Chicago, IL). A P value < 0.05 was considered significant.

Table 1. Patient Characteristics and the recurrence of Atrial Fibrillation after Pulmonary Vein Catheter Ablation

Variable	No recurrence of AF (n = 49)	Recurrence of AF (n = 16)	P value
Age (years)	62 ± 10	59 ± 10	p = N.S.
Male	38 (78%)	15 (94%)	p = N.S
History of diabetes	7 (14%)	2 (13%)	p = N.S
History of hypertension	23 (47%)	8 (50%)	p = N.S
BMI	23.7 ± 2.89	26.3 ± 2.68	p = 0.002
Echocardiographic findings			
Left ventricular ejection fraction (%)	61.5 ± 7.9	59.2 ± 7.7	p = N.S
Deceleration time (msec)	205 ± 46	206 ± 49	p = N.S
Resting hemodynamics			
Resting HR (bpm)	66 ± 9	66 ± 7	p = N.S
Resting systolic BP (mmHg)	132 ± 12	123 ± 11	p = N.S
Resting diastolic BP (mmHg)	73 ± 9	72 ± 9	p = N.S
Laboratory data			
CRP (mg / dl)	0.3 ± 0.4	0.2 ± 0.1	p = N.S.
BNP (pg / dl)	70.3 ± 79.6	87.5 ± 91.2	p = N.S.
Medications			
Use of angiotensin-converting enzyme inhibitor	15 (31%)	7 (44%)	p = N.S
Use of beta-blocker	11 (22%)	3 (18%)	p = N.S
Use of calcium channel antagonist	14 (29%)	3 (19%)	p = N.S
Use of digoxin	9 (18%)	2 (13%)	p = N.S
Use of diuretic drug	3 (6%)	3 (19%)	p = N.S
Quantitative MDCT data			
Left atrial dimension (ml)	125.8 ± 36.9	91.1 ± 27.1	$p < 0.0001$
Right atrial dimension (ml)	117.5 ± 40.9	71.6 ± 25.5	$p < 0.0001$

Abbreviation : BMI = Body Mass Index, HR = Heart rate, BP = Blood pressure, CRP = Serum concentration of C-Reactive Protein, BNP = the plasma Brain Natriuretic Peptide level, MDCT = Multi-detector Computed Tomography, N.S = Not Significant.

Results

Patient Characteristics

Over the 6-month follow-up, 16 patients showed recurrence of AF (24.6%), and 49 patients had no recurrence. The patients with AF recurrence showed significantly larger RA and LA volumes than the patients without recurrence, but there were no significant differences between the patients with and without recurrence of AF in age, gender, cardiovascular risk factors, and hemodynamic responses (Table 1). Body mass index was higher in the patients with AF recurrence than in those without, but these risk factors such as obesity and hypertension were controlled by diet, salt restriction, and medication after the start of this study. No patients had a history of alcohol abuse, genetic factors, or sleep apnea. There was no significant difference between the group in inflammatory markers such

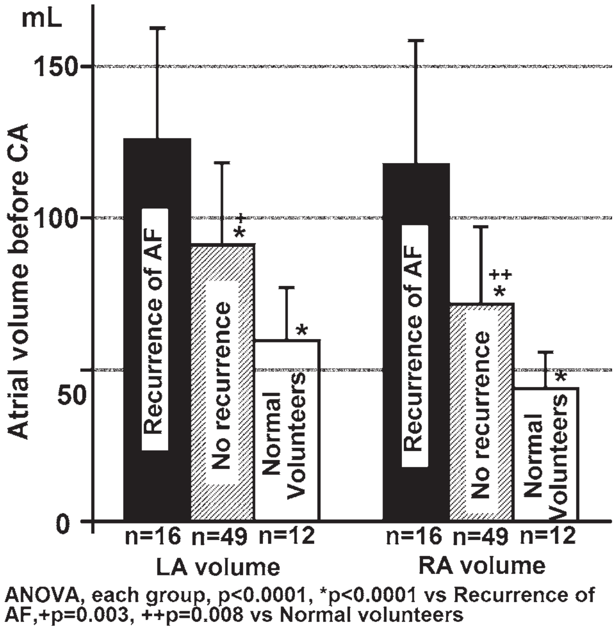

Fig. 3. Comparison of left atrial (LA) and right atrial (RA) volumes between idiopathic paroxysmal AF patients with and without recurrence of AF and normal healthy volunteers.

as serum C-reactive protein or neurohumoral biomarkers such as plasma brain natriuretic peptide. No medications were associated with the recurrence of AF.

Before CA, both atrial volumes were significantly larger in the AF patients than in normal volunteers (LA : 99.7 + 33.2 ml vs. 59.7 + 17.4 ml, and RA : 82.9 + 35.7 ml vs. 43.9 + 12 ml). Further, both RA and LA volumes were associated with the recurrence of AF (LA : 125.8 + 36.9 ml in patients with AF recurrence vs. 91.1 + 27.1 ml in 49 patients without recurrence, and RA : 117.5 + 40.9 ml vs 71.6 + 25.5 ml, respectively) (Fig. 3).

LA and RA Volumes for Predicting the Recurrence of AF

Optimal thresholds for predicting the recurrence of AF were at LA volume = 99.4 ml and RA volume = 87.6 ml (Fig. 4). The sensitivity of increased LA volumes (> 100 ml) for predicting the recurrence of AF was 81.3 % in 13 of 16 patients with recurrence, and the specificity was 69.4% in 34 of 49 patients without recurrence of AF. The sensitivity of increased RA volumes (> 87 ml) was 81.3% in 13 of 16 patients with recurrence, and the specificity was 75.5% in 37 of 49 patients without recurrence of AF. Further, LA and RA volumes were closely correlated ($r = 0.404$, $P = 0.001$). In multivariate analysis, both LA and RA volumes were independent and significant predictors of successful CA with hazard ratios of 9.8 [95 % CI 2.4 to 39.6] and 13.4 [95 % CI 3.2 to 54.9] after adjustment for potential confounding variables such as age, gender, coronary risk factors, and medications.

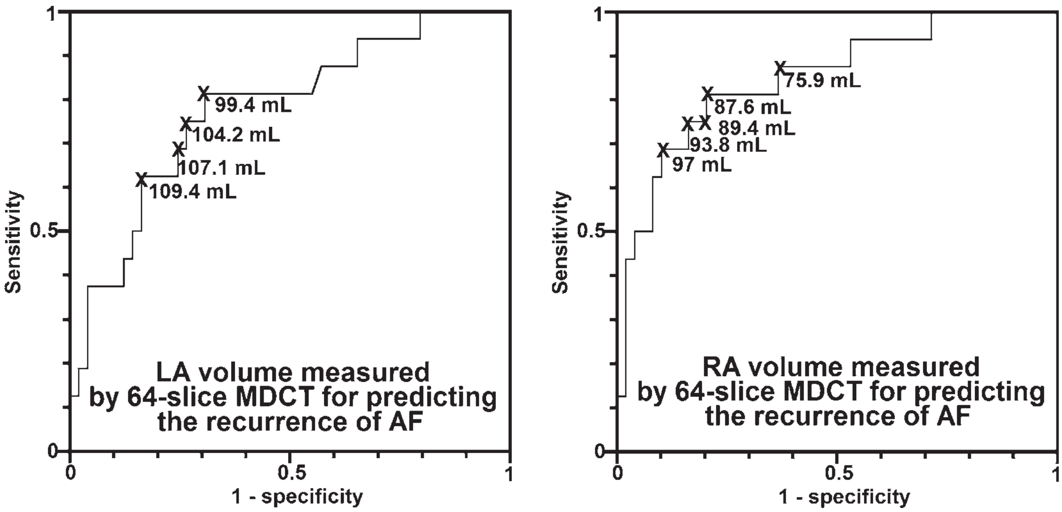

Fig. 4. Receiver operating characteristics (ROC) curve. Success after catheter ablation of AF for left atrial (LA) and right atrial (RA) volumes measured by 64-multislice detector computed tomography (MDCT).

Table 2. Prediction of the Recurrence of Atrial Fibrillation after Pulmonary Vein Catheter Ablation According to Multivariate Analysis

Variable	Success CA (%)		Odd ratio	Wald	P value
	Present	Absent	(95% CI)	χ^2	
Large LA volume (> 100 ml)	13 / 28 (46.4%)	3 / 37 (8.1%)	9.8 (2.4–39.6)	10.3	$p = 0.001$
Large RA volume (> 87 ml)	13 / 25 (52%)	3 / 40 (7.5%)	13.4 (3.2–54.9)	12.9	$p < 0.0001$

Abbreviations : CA = Catheter ablation, CI = Confidence interval, LA = Left atrium, RA = Right atrium.

Discussion

This study demonstrated that RA volume measured by MDCT could predict the recurrence of AF after CA with a sensitivity and specificity similar to LA volume measurement.

LA size is an established predictor of AF recurrence and maintenance after electrical cardioversion because AF induces electrical and structural remodeling of the fibrillating atria, perpetuating AF[3, 4]. However, the significance of RA volume was not clarified in previous studies despite both volumes increasing symmetrically in patients with AF[13]. In a 6-month follow-up study by ECG in patients with AF, Shin *et al*[18] found that LA volume increases over 34 ml / m^2 predicted recurrence of AF after CA with a sensitivity of 70% and specificity of 91%. However, the same study concluded that RA volume measurements were less significant predictors of AF recurrence by multivariate analysis. Their study was new and noteworthy in even suggesting the use of RA volume for predicting AF recurrence after CA, but it had some limitations. First, the evaluation did not separate paroxysmal AF and permanent AF. Paroxysmal AF is frequently a purely trigger-dependent phenomenon, whereas permanent AF is mechanistically complex, implicating a more diffuse abnormality of the atrial substrate[4]. Second, the ECG could not always accurately measure atrial enlargement due to multivariate variations in the atrium, and in particular, the right atrium[19]. Therefore, we used MDCT in the current study because it quantifies atrial volume 3 dimensionally[19]. Helms *et al*[11] also showed in a 12-month follow-up study using MDCT that large LA volume (> 135 ml) is a predictor of AF recurrence with a sensitivity of 36% and specificity of 96% ; however, their study subjects also included patients with permanent AF.

To our knowledge, we present herein the first quantitative evaluation of both left and right atrial volumes for predicting the recurrence of AF after CA using MDCT and quantitative three-dimensional measurement software. The sensitivity of prediction for large LA volumes (> 100 ml) was 81.3%, and the specificity was 69.4% in patients with paroxysmal AF. More importantly, the sensitivity of prediction for large RA volumes (> 87 ml) was 81.3% and the specificity was 75.5%. In addition, the precise three-dimensional atrial reconstruction by the OsiriX software allows for a computer-aided and navigation-aided quantitative measurement of atrial volume[16,17]. AF is maintained by microreentrant sources located in the LA[20,21] with fibrillatory conduction toward the RA[22]. Therefore, the RA was thought to be a bystander during maintenance or recurrence of AF, while the LA underwent a change typical of both paroxysmal and permanent AF. Recently, we reported the significance of sympathetic nervous system abnormality for predicting perpetuated AF in patients with paroxysmal AF[23], and the magnitude of nerve sprouting and hyperinnervation has been reported to be higher in the RA than in the LA in a canine model of AF produced by prolonged RA pacing, further suggesting the significance of RA[24]. The percentage area occupied by fibrosis was also recently shown to be higher in the LA than in the RA of patients who developed AF, suggesting more reversible and quick changes to the right atrium[25]. Our result thus confirms that RA volume is important for morbidity in patients with AF. Finally, MDCT is a guide to invasive intervention in patients with coronary artery disease[26,27] and rhythm disorders[14], and our results indicated the significance of three-dimensional and quantitative evaluation of RA size using a computer-aided technique with 64-slice MDCT.

The present study compared atrial volumes with those measured similarly in previous studies with respect to the recurrence of AF[1,4,13,28]. Other studies used the value of atrial volume indexed to body mass or body surface area[18]. Obesity is an important risk factor for the development of AF, while body weight is closely correlated to LA volume, and weight reduction has been linked to regression of LA enlargement[4,29]. Furthermore, the atrial volume index correlated by body mass or body surface area was less significant compared to the value of direct atrial volume measurement used herein and elsewhere because the atrial volumes were independent of body mass value[28]. Similarly, we did not use the weight index because atrial volume correlated with body mass index in the present study.

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