Evaluation of Left Atrial and Left Ventricular Function during and between Atrial Fibrillation Episodes by Using Dual-Source Computed Tomography

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Objective: Previous studies assessing left atrium (LA) function in patients with atrial fibrillation (AF) have not simultaneously analyzed left ventricle (LV) function. To evaluate differences in LA and LV volume and function in patients with AF during and between AF episodes compared to healthy subjects by using dual-source computed tomography (DSCT).

Materials and Methods: Sixty-one consecutive patients with AF and 30 healthy subjects underwent retrospective electrocardiography-gated DSCT. Thirty of 61 AF patients experienced AF during scan acquisition (AF episode subgroup), and 31 were in sinus rhythm (AF non-episode subgroup). LA and LV functions were analyzed with dedicated software and groups were compared with analysis of variance and least significant difference test.

Results: The maximal LA volumes in healthy subjects, the AF episode subgroup, and the no AF episode subgroup were 94.4 ± 19.9 mL, 121.8 ± 42.4 mL, and 101.4 ± 32.9 mL, respectively ($p=0.005$). Left ventricular end-diastolic volumes (LVEDV) in healthy subjects, the AF episode subgroup and the no AF episode subgroup were 160.5 ± 34.4 mL, 131.7 ± 37.3 mL, and 138.1 ± 27.6 mL, and respectively ($p=0.003$). Left ventricular end-systolic volumes were 55.6 ± 19.4 mL, 65.2 ± 32.4 mL, and 51.0 ± 14.9 mL, respectively ($p=0.060$). Increased LA volume, decreased LVEDV, and decreased LA and LV systolic function were found during AF episodes.

Conclusion: Our data contributes to understanding the mechanism of AF and guides clinical management of patients with AF.

Key words Atrial fibrillation · Left atrium · Left ventricle · Computed tomography.

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INTRODUCTION

The left atrium (LA) receives oxygenated blood from the pulmonary veins and pumps it through the mitral valve into the left ventricle (LV). Thus, the LA influences LV filling and

perpetuates the stroke volume [1].

During atrial fibrillation (AF), LA function is lost due to asynchronous atrial activity, irregular ventricular responses, and the resulting rapid heart rate (HR) [2]. Because it adversely affects LA function, AF can lead to cardiac remodeling and LA dilation. LA enlargement is an important predictor of AF recurrence following electrical cardioversion [2].

Previous studies assessing LA function in patients with AF

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[3,4] have not simultaneously analyzed LV function. Our hypothesis was that AF adversely affects both LA and LV volume and function and that these parameters are at least partially restored when a patient re-enters sinus rhythm. Therefore, the aim of our study was to investigate LA and LV volume and function by using dual-source computed tomography (DSCT) in patients with AF during and between AF attacks and to compare these values with healthy control subjects. These measurements may help to manage AF patients.

MATERIALS AND METHODS

This retrospective study was approved by the Medical Ethics Committee of Fu Wai Hospital, Peking Union Medical College & Chinese Academy of Medical Sciences (2017-926). The written informed consent was obtained from all patients.

Study design and patient population

We enrolled 61 consecutive patients with AF who successfully underwent cardiac computed tomography (CT). All 61 patients had been diagnosed with AF by electrophysiologists. They were referred for cardiac CT to evaluate coronary arteries and pulmonary veins and to exclude thrombus before radiofrequency ablation treatment. Patients with unsuccessful DSCT scans or blurred contours of the heart chambers were excluded. Electrocardiography (ECG) signals were recorded during the CT exams, and a cardiologist determined the presence of AF. Thus, patients were retrospectively divided into 2 subgroups: 1) patients who experienced an AF episode during the CT scan (AF episode subgroup, $n=30$) and 2) patients who were in sinus rhythm during the CT scan (no AF episode subgroup, $n=31$).

To establish a control group, we included 30 consecutive non-AF patients who underwent cardiac CT to rule out coronary artery disease during the same period and who had no morphological or functional abnormalities detected (control group, $n=30$). Patient characteristics are summarized in Table 1.

Patients were scanned with a retrospectively ECG-gated DSCT scan protocol and included in the study if they met the following criteria: 1) the absence of abnormal cardiac or pulmonary findings, except for abnormal cardiac findings caused by AF;

2) sufficient opacification of LA and LV chambers to evaluate cardiac function; and 3) sufficient ECG signal quality during the CT scan.

CT acquisition protocol

All patients were scanned on a DSCT scanner (SOMATOM Definition, Siemens Healthcare, Forchheim, Germany) with a retrospectively ECG-gated coronary CT angiography protocol. The scan was started 20 mm below the bifurcation of trachea and ended at the level of the diaphragm. The tube voltage was 80–120 kV depending on the patient's body mass index (BMI), and the tube current-time was 350–420 mAs with the tube current modulation technique. The acquisition collimation was $2 \times 32 \times 0.6$ mm. The pitch was 0.2–0.5 with HR adaptation.

The ECG signal, mean HR, and HR variation during the scan were recorded for every patient. The ECG signal was stored as a Digital Imaging and Communication in Medicine image to evaluate heart rhythms. The CT dose index in volume and dose length product (DLP) were recorded from the CT console. The effective dose was calculated by multiplying the DLP by a chest conversion coefficient [$k=0.014$ mSv/(mGy $\times$ cm)] [5].

The contrast medium [Ultravist 370 (370 mg/mL), Bayer Pharma, Germany, or Omnipaque 350 (350 mgI/mL), GE Healthcare, Shang Hai, China] was injected intravenously via a 20-gauge trocar with a dual-head power injector (CT Stellant, Medrad, Indianola, IA, USA). A tri-phasic injection protocol was used: phase I, 50–60 mL contrast material; phase II, 30 mL mixture of contrast material and saline in a 30:70 ratio; phase III, 40 mL saline. The injection speed was 4.0–5.5 mL/s for all phases. The bolus tracking technique was used. For this purpose, a region of interest (ROI) was placed inside the LA and the scan was automatically triggered 6 seconds after the ROI reached a 100-Hounsfield unit threshold.

Image reconstruction

All images were reconstructed with the following parameters: 0.75-mm slice thickness, 0.4-mm increment, medium soft kernel of B25f, 180-mm field of view, and 83-ms temporal resolution. Cardiac images were reconstructed into 20 cardiac phases with a 5% R-R interval difference during the cardiac cycle. All images

Table 1. Patient characteristics

	Control group (n=30)	AF episode subgroup (n=30)	AF non-episode subgroup (n=31)	F/ χ^2	p-values
Male, n (%)	19 (63.3)	22 (73.3)	16 (51.6)	3.08 (χ^2)	0.21
Age (years)	51.6 $\pm$ 12.0	51.9 $\pm$ 11.2	51.5 $\pm$ 13.4	0.01	0.99
BMI (kg/m ²)	24.9 $\pm$ 3.5	24.9 $\pm$ 2.8	23.9 $\pm$ 3.4	0.89	0.42
BSA (m ²)	1.8 $\pm$ 0.2	1.8 $\pm$ 0.2	1.8 $\pm$ 0.5	0.26	0.77
HR (bpm)	66.1 $\pm$ 12.7	80.0 $\pm$ 18.0	70.4 $\pm$ 19.3	5.29	<0.01
HR variation (bpm)	5.0 $\pm$ 2.2	63.4 $\pm$ 25	4.3 $\pm$ 2.2	165.30	<0.01

χ^2 means statistical analyses were performed one-way ANOVA (F) and χ^2 test (χ^2). AF: atrial fibrillation, BMI: body mass index, BSA: body surface area, HR: heart rate

were transferred to a commercial workstation for cardiac function analysis (AW 4.4, GE Healthcare, Milwaukee, WI, USA).

Analysis of cardiac function

To analyze cardiac function, the endocardium of the LA and LV was manually delineated by two experienced radiologists who were blinded to patients' identifying information in case of significant error. The LA volume included the region above the mitral valve but excluded the pulmonary vein at its junction with the LA, as has been proposed previously [6,7]. The LA appendage could be accurately reconstructed in all patients, hence was included in the volumetric analysis. Long- and short-axis images of the ventricle were calculated in 5% intervals of the cardiac cycle, as has been proposed previously [8]. An example of LA segmentation is given in Fig. 1A-D. The LV was defined as the volume enclosed by the mitral valve, aortic valve, and myocardial wall. An example of LV segmentation is given in Fig. 1E-H. The cardiac phase immediately before mitral valve closure was defined as the end-diastolic volume of the LV. The cardiac phase immediately before mitral valve opening was defined as the end-systolic volume of the LV.

The cardiac function of the LA and LV were quantified with

the following equations [1]:

1) $LACV = LVS - LAS$ (where LACV is the LA conduit volume, LVS is the LV stroke volume, and LAS is the LA stroke volume);

2) $LARV = LAV_{max} - LAV_{min}$ (where LARV is the LA reservoir volume = LA stroke volume, LAVmax is the maximum LA volume, and LAVmin is the minimum LA volume);

3) $LAEF = (LAV_{max} - LAV_{min}) / LAV_{max}$ (where LAEF is the LA ejection fraction);

4) $LVS = LVEDV - LVESV$ (where LVS is the LV stroke volume, LVEDV is the LV end-diastolic volume, and LVESV is the LV end-systolic volume);

5) $LVEF = LVS / LVEDV \times 100\%$ (where LVEF is the LV ejection fraction).

Measurement of left atrial and left ventricular diameters and cross-sectional areas

We further assessed whether axial diameter and area are sufficient to assess volume differences. The LA and LV diameters were measured with digital calipers on axial images. The two longest perpendicular diameters were measured in the cardiac phase when LA and LV reached the maximum volume [1-3].

Fig. 1. Representative patient. Images and analysis are shown for a 52-year-old female patient who was 178 cm tall and weighed 70 kg and had an AF episode during the DSCT scan. BSA was 1.9 m². Her heart rate during the DSCT scan was 74–151 bpm. Although the LA maximal volume did not increase (94.4 mL, vs. 94.4±19.9 mL in the control group), the minimal volume increased significantly (80.6 mL, vs. 45.9±16.4 mL in the control group). LA reservoir volume and conduit volume decreased (13.8 mL vs. 48.4±9.4 mL in the control group and 38.5 mL vs. 56.4±21.5 mL in the control group, respectively). LA ejection fraction also decreased significantly (14.6% vs. 52.3±9.1% in the control group). LV end-diastolic volume decreased significantly (109.9 mL vs. 160.5±34.4 mL in the control group). LV end-systolic volume did not change significantly (57.6 mL compared to 55.6±19.4 mL in the control group). LV ejection fraction decreased significantly (47.6% vs. 65.8±7.2% in the control group). (C) and (G) are multi-planar reformations of the LA and LV, respectively. Volume curves for the LA and LV in (D) and (H) were automatically generated by the workstation when measuring LA and LV volume, respectively. A: Vertical section of LA. B: Transverse section of LA and LAA. C: Three-dimensional reconstruction of LA and LAA. D: The volume-time curve of LA. E: Vertical section of LV. F: Transverse section of LV across mitral valve. G: Three-dimensional reconstruction of LV. H: The volume-time curve of LV. PV: pulmonary vein, LA: left atrium, LV: left ventricle, LAA: left appendage, AO: aorta, MV: mitral valve, ES: end-systolic volume, ED: end-diastolic volume, AF: atrial fibrillation, DSCT: dual-source computed tomography, BSA: body surface area.

The product of the two longest diameters was used as the cross-sectional area of the LA or LV.

Statistical analysis

All statistical analyses were performed with a commercial software package (SPSS 19.0; IMB Corp., Armonk, NY, USA). Categorical data, such as sex, were presented as frequencies and percentages, and differences were tested with the χ^2 test. Continuous data, such as age, were presented as mean $\pm$ standard deviation and analyzed with one-way analysis of variance or least significant difference tests. A p-value<0.05 was considered statistically significant. Pearson correlation coefficient (R) was used to quantify the relationship between LAEF and LVEF depending on LA and LV synchronization in the AF episode subgroup. R=0–0.1 no correlation, R=0.1–0.3 weak correlation, R=0.3–0.5 medium correlation, R=0.5–1.0 significant correlation.

RESULTS

Comparison of patient characteristics

Our study included 57 males and 34 females with an average age of 51.6 $\pm$ 12.1 years (range 18–77 years) (Table 1). The three study groups had no significant differences in sex distribution (p= 0.21), age (p=0.99), BMI (p=0.42), or body surface area (p= 0.77) (Table 1). The average HR during CT scans was 66.1 $\pm$ 12.7 bpm (range 32–94 bpm) in the control group, 80.0 $\pm$ 18.0 bpm (range 51–121 bpm) in the AF episode subgroup, and

70.4 $\pm$ 19.3 bpm (range 42–128 bpm) in the no AF episode subgroup. HR variation during CT scans was 5.0 $\pm$ 2.2, 63.4 $\pm$ 25, and 4.3 $\pm$ 2.2 bpm in control, AF episode, and no AF episode groups, respectively. Mean HR and HR variation differed significantly between the AF episode and no AF episode subgroups (p=0.030 and p<0.001, respectively), but the control and no AF episode groups did not differ significantly (p=0.319 and p=0.856, respectively). Patient characteristics are listed in Table 1.

Effective radiation dose

The effective radiation doses were 11.8 $\pm$ 3.8 mSv, 23.6 $\pm$ 6.5 mSv, and 11.9 $\pm$ 3.0 mSv in the control, AF episode, and no AF episode groups, respectively. These effective doses differed significantly different between the AF episode and no AF episode subgroups (p<0.001) and between the control and AF episode groups (p<0.001). The control and no AF episode groups did not differ significantly (p=0.959).

Cardiac function

LA and LV volumes and functional parameters are presented in Table 2 and 3, Fig. 2. The AF episode subgroup had significantly higher LAVmax and LAVmin, and lower LVSV and LAEF than the control group (all p<0.01). The no AF episode subgroup had significantly higher LAVmin, and lower LVSV and LAEF than the control group. LAVmax did not differ significantly from the control group (p=0.409). LVEDV did not differ significantly between the AF episode and no AF episode subgroups

Table 2. Left atrial function and volume in each group

Subgroup	Control group (n=30)	AF episode subgroup (n=30)	AF non-episode subgroup (n=31)	p-values	p-values*	p-values†	p-values‡
LAVmax (mL)	94.4 $\pm$ 19.9	121.8 $\pm$ 42.4	101.4 $\pm$ 32.9	0.005	0.002	0.409	0.016
LAVmin (mL)	45.9 $\pm$ 16.4	95.1 $\pm$ 41.3	65.8 $\pm$ 31.5	<0.001	<0.001	0.016	<0.001
LACV (mL)	56.4 $\pm$ 21.5	39.7 $\pm$ 13.9	51.5 $\pm$ 19.5	0.003	0.008	0.325	0.082
LARV (mL)	48.4 $\pm$ 9.4	26.8 $\pm$ 15.4	35.6 $\pm$ 12.5	<0.001	0.921	0.010	0.013
LAEF (%)	52.3 $\pm$ 9.1	23.7 $\pm$ 13.6	37.4 $\pm$ 13.3	<0.001	<0.001	<0.001	<0.001

*p value of difference between the control group and the AF episode subgroup, †p value of difference between the control group and the AF non-episode subgroup, ‡p value of difference between the AF episode subgroup and the AF non-episode subgroup. LAV: left atrial volume, LACV: left atrial conduit volume, LARV: left atrial reservoir volume, LAEF: left atrial ejection fraction, AF: atrial fibrillation

Table 3. LV function and volume in each group

	Control group (n=30)	AF episode subgroup (n=30)	AF non-episode subgroup (n=31)	p-values	p-values*	p-values†	p-values‡
LVEDV (mL)	160.5 $\pm$ 34.4	131.7 $\pm$ 37.3	138.1 $\pm$ 27.6	0.003	0.001	0.009	0.509
LVESV (mL)	55.6 $\pm$ 19.4	65.2 $\pm$ 32.4	51.0 $\pm$ 14.9	0.060	-	-	-
LVSV (mL)	104.9 $\pm$ 22.3	66.5 $\pm$ 17.5	87.1 $\pm$ 19.6	<0.001	<0.001	<0.001	0.001
LVEF (%)	65.8 $\pm$ 7.2	52.3 $\pm$ 12.0	62.9 $\pm$ 7.3	<0.001	<0.001	0.699	<0.001

*p value of difference between the control group and the AF episode subgroup, †p value of difference between the control group and the AF non-episode subgroup, ‡p value of difference between the AF episode subgroup and the AF non-episode subgroup. LVEF: left ventricular ejection fraction, LVEDV: left ventricular end-diastolic volume, LVESV: left ventricular end-systolic volume, LVSV: left ventricular stroke volume, AF: atrial fibrillation

($p=0.509$), but it was significantly higher in the control group ($p<0.01$). LVSV differed significantly among all 3 groups ($p<0.001$). LVEF was significantly lower in the AF episode subgroup than in both the control and no AF episode groups (all $p<0.001$), but the control and no AF episode groups did not differ ($p=0.699$). LVESV did not differ among the 3 groups ($p=0.060$). LAEF and LVEF were significantly correlated ($R=0.515$) depending on LA and LV synchronization in the AF episode subgroup.

Fig. 2. LA and left ventricular volume changes over the cardiac cycle. The change in LA and LV mean volumes during the cardiac cycle are shown. LA volume increased and LA systolic function decreased during AF attacks, but partly recovered during sinus rhythm. LV end-diastolic volume decreased and LV systolic function decreased during AF episodes but partly recovered during sinus rhythm. Left ventricular end-systolic volumes in the control group was lower than in the AF episode subgroup and higher than in the no AF episode subgroup. Hence, LV ejection function was maintained by enhanced contraction during sinus rhythm. LA: left atrial, LV: left ventricle, AF: atrial fibrillation.

Axial diameters and cross-sectional areas of the LA and LV

Table 4 lists the diameters and cross-sectional areas of the LA and LV in all groups. The LV cross-sectional area differed significantly between the AF episode and control groups and between no AF episode and control groups (both $p<0.01$).

DISCUSSION

The principal function of the LA is to modulate LV filling; thus, influences cardiac performance [1]. The LA serves multiple functions: it acts as a reservoir during systole, a conduit during early diastole, and a pump during late diastole [1,9]. The reservoir function of the LA consists of LA filling during systole and is regulated by atrial compliance [3,10]. In patients with AF, mechanical remodeling of the LA manifests as decreased atrial contractility and increased atrial compliance, which lead to LA enlargement [3,11,12]. As a result, the LA primarily serves as a conduit in these patients [13].

Recently, Park et al. [3] studied structural remodeling of the LA in patients with AF by using 64-multislice cardiac CT. They found that the anatomical compartments of the LA play different roles in patients with AF. The LA appendage has the highest contractility and serves an independent function, whereas the venous LA plays a smaller role in LA function. In our study, we analyzed the whole LA instead of dividing it into compartments. Our results might promote using DSCT for clinically accurate evaluation of AF.

DSCT is an important tool for evaluating both LA and LV function in patients with severe arrhythmia [14], including AF [7,15], and in patients with sinus rhythm [1,8,16,17]. LA and LV function and volume measurement were reported to be comparable between DSCT, echocardiography and cardiac magnetic resonance [1,14]. DSCT angiography is an important tool to illustrate the anatomy of LA and pulmonary veins in patients with AF before catheter ablation [7]. DSCT for evaluating heart function allows for advantageous volumetric rendering, thin slice scans, and reliable data with good imaging. A previous

Table 4. Diameters and cross-sectional area of left atrium and left ventricle

	Control group (n=30)	AF episode subgroup (n=30)	AF non-episode subgroup (n=31)	p-values
LA				
Lateral diameter (cm)	6.0±0.9	6.5±1.3	6.5±1.2	0.173
Anteroposterior diameter (cm)	3.6±0.7	3.8±0.8	3.6±0.8	0.371
Cross-section area (cm ²)	21.5±4.9	25.7±9.1	23.8±8.7	0.124
LV				
Long-axis diameter (cm)	8.1±1.3	8.1±0.8	7.9±0.8	0.612
Short-axis diameter (cm)	4.0±0.4	3.9±0.8	3.9±0.6	0.863
Cross-section area (cm ²)	32.2±6.6	32.4±8.2	30.7±6.0	<0.001

LA: left atrial, LV: left ventricle, AF: atrial fibrillation

study evaluated LV and LA volume and function with DSCT [18], but it did not include patients with AF. Other studies assessed LA function in patients with AF [3,4] but did not simultaneously analyze LV function. Simultaneously evaluating LA and LV in patients with AF provides a more comprehensive functional analysis than evaluating LA function alone.

Therefore, our study investigated LA and LV function in patients with AF by using DSCT before radiofrequency ablation. Our results show that during AF, the LACV, LARV, and LAEF decreased, and LAVmax, LAVmin, and LVEDV increased compared with the control group. These findings are consistent with previous reports [2,6,19].

By comparing the AF episode and control groups, our results show that the functions of both the LA (LAEF) and LV (both stroke volume and ejection fraction) decrease during AF episodes. This result indicates lost synchronization of LA and LV contraction during atrial fibrillation. By comparing these functional parameters among the control, AF episode, and no AF episode groups, we conclude that LA and LV function partly recover upon restored sinus rhythm. A similar conclusion on LA volume and function can be drawn by analyzing data from Park et al. [3], though the authors did not emphasize this point.

Comparing axial diameters and cross-sectional areas of the LA and LV showed that only the LV area differed significantly among the AF episode, no AF episode, and control groups. This result suggests that volumetric analysis is more sensitive for evaluating LA and LV function than are diameter and area.

The results of this study have to be considered in the context of the study design. The number of patients in each subgroup was limited. The AF episode and no AF episode subgroups comprised different patient populations. Capturing AF and non-AF data from each patient would be unethical due to the relatively high radiation exposure associated with retrospectively gated cardiac CT. Rather, we compared patients with an AF episode or no episode at the time of the scan. This design introduces a potential bias because patients with more frequent or prolonged episodes are more likely to be in AF during the scan. The degree of cardiac remodeling in AF likely depends on the frequency of AF attacks and may be confounding. Also, we did not correlate functional parameters with radiofrequency ablation outcomes. Further studies are warranted to investigate whether the analysis presented in our study can be used to predict the success of radiofrequency ablation.

In conclusion, we found that dual-source CT can be used to simultaneously assess LA and LV function in patients with AF. During an AF episode, we found an increased LA volume and decreased LVEDV, as well as decreased LA and LV systolic function.

Conflicts of Interest

Run-Ze Wu is an employee of Siemens Healthcare. Joseph U Schoepf is a consultant for and receives research support from Bayer, Bracco, GE, Medrad

and Siemens. The other authors have no industry relationships or conflicts of interest relevant to this investigation to disclose.

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