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Diagnostic Performance of Left Atrial Diameter Measurement in Computed Tomography to Detect Increased Left Atrial Volume

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Abstract. *Background/Aim: The left atrium (LA) is frequently imaged in cardiac computed tomographic (cCT) examinations. The LA volume can be accurately measured with three-dimensional (3D) volumetry but this method is time consuming and thus not routinely used in clinical practice. Accordingly, increased LA size may be overlooked although volume enlargement is associated with adverse cardiovascular events. We evaluated the accuracy of LA diameter measurement in cCT and in transthoracic echocardiography (TTE) in the diagnosis of LA enlargement using 3D cCT as the reference standard. Patients and Methods: Altogether, 146 patients with suspected cardiogenic stroke underwent cCT and TTE. LA volume by cCT was determined for all patients. LA diameter was measured in both modalities. Furthermore, 40 healthy controls were analyzed in order to assess the cut-off values for normal LA volume. Diagnostic performance of cCT and conventional TTE diametrical measurements for detecting enlarged LA volume were analyzed and compared using Cohen's kappa (κ). Results: In controls, the mean LA volume was 59.8±15.3 ml and the mean LA diameter was 30.4±5.0 mm by cCT. The mean value plus twice the standard deviation, which was considered the upper limit, for normal LA volume and diameter were 90.4 ml and 40.4 mm, respectively. Age- and gender-matched patients with stroke had statistically significantly (p<0.001) larger LA volumes (85.5±21.1 vs. 59.8±15.3 ml) and diameters (37.6±5.7 vs. 30.4±5.0 mm) than controls. LA diameter measurement by cCT was more reliable in detecting an LA volume enlargement than the corresponding measurement with TTE (κ=0.489 vs. 0.234; p=0.002). Conclusion: An enlarged LA diameter measured by cCT was more reliable than TTE at detecting enlarged LA volume.*

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It has been well-documented that dilatation of the left atrium (LA) is associated with adverse cardiovascular events such as atrial fibrillation (AF), coronary artery disease, congestive heart failure, myocardial infarction, stroke, and death (1-11). In routine clinical practice, LA size is conventionally assessed by transthoracic echocardiography (TTE) as the maximal antero-posterior diameter (APd) of the LA measured with two-dimensional (2D) echocardiography guided M-mode at ventricular end-systole. Values for LA APd of <38 mm for women and <40 mm for men are considered normal according to the guidelines of the American Society of Echocardiography (ASE) (1). Because of its simplicity and wide accessibility, the TTE M-mode LA APd is extensively used in clinical settings.

Computed tomography (CT) is widely applied for cardiological indications such as non-invasive coronary angiography (12-15). Previous studies have shown that LA volume can be accurately measured with CT using three-dimensional (3D) volumetry, in which the LA contours are defined in consecutive slices and the true 3D volume is estimated by summation of the areas in separate slices (16, 17). Recently cardiac CT (cCT) was shown to be a promising method for the evaluation of patients with suspected cardioembolic stroke or transient ischemic attack (TIA) (18).

Although highly reliable, this method is time-consuming and thus not routinely used in clinical practice (18). We studied how reliable estimation of values of LA APd by TTE and cCT would be in detecting LA volume enlargement.

Patients and Methods

Patients. This is a part of the prospective, single-center observational study. All patients admitted to our University Hospital between February 2005 and November 2009 with suspected cardioembolic stroke/TIA were candidates for the study. These patients had no previously known AF nor did they experience AF during their stay in the hospital. The study was approved by the Kuopio University Hospital Research Ethics Board (approval number 82/2004) and all clinical investigations were conducted according to the principles expressed in the Declaration of Helsinki. Before participating in the study, written informed consent was obtained from the patient or from the patient's legally authorized representative if the patient was not able to provide consent because of impaired mental or physical capacity caused by stroke/TIA.

Ultimately 146 out of the initially 162 recruited patients were included in the study. Sixteen patients were excluded: four patients had poor image quality in cCT, three lacked electrocardiography synchronization, three refused to participate after having previously consented, three did not undergo TTE and in two patients, the contrast medium failed, while one patient suffered from renal dysfunction (19).

The presence of hypertension (previous diagnosis of hypertension with drug treatment) and patients' body mass index [BMI; the ratio of weight (kg) to squared height (m^2)] were determined to be used as confounding factors.

Controls. With respect to controls, we retrospectively analyzed the 243 consecutive patients who had undergone coronary CT-angiography (CTA) at our University Hospital between December 2008 and July 2011. Patients without cardiovascular diseases or previous stroke/TIA who had undergone coronary CTA were identified. Finally, a group of 40 healthy controls (21 males; mean age=54±9 years, range=32-74 years) was found suitable for an age- and gender-matched control population for pairwise comparison with stroke/TIA patients. Cut-off values for an enlarged mid-diastolic LA volume and enlarged LA APd at the level of aortic bulb were defined as two standard deviations (2SD) above the mean in the control population (19).

Diametric measurements with TTE. Echocardiographs were obtained (M4S 3 MHz probe; GE Medical Systems, Chalfont St. Giles, Buckinghamshire, UK) and analyzed by several cardiologists as a part of their routine clinical work (17). The time interval between cCT and TTE was 0.9±4.5 days. The LA APd assessment by TTE was performed using the parasternal long-axis view. The LA APd was measured during ventricular end-systole from the 2D-guided M-mode following the recommendations of the ASE. Values of LA APd <38 mm in women and <40 mm in men are considered normal (1). The aortic root and the LA were identified using the 2D mode. After the LA had been identified, the M-mode cursor was directed so as to be perpendicular to the aortic root and the M-mode image was used to measure the maximal LA APd as the distance from the trailing edge of the posterior aortic wall to the leading edge of the posterior LA wall.

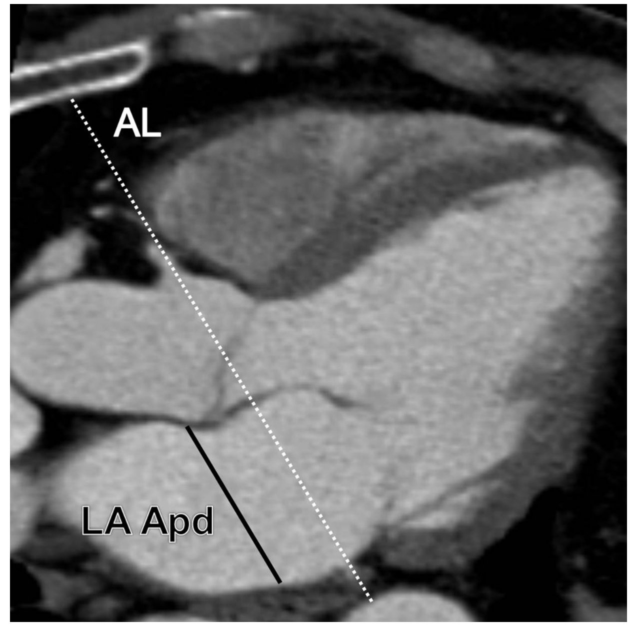

Figure 1. *The left atrial antero-posterior diameter (LA APd) was measured from a three-chamber view in ventricular mid-diastole. An auxiliary line (AL), traversing the entire left atrium, was drawn perpendicular to the left ventricular outflow tract. Parallel to the AL, the LA APd was measured at the level of the aortic bulb.*

Diametric and volumetric measurements with computed tomography. Contrast-enhanced cCT (Somatom Sensation 16 or Somatom Definition AS; Siemens Medical Solutions, Forchheim, Germany) was performed at mid-diastole (17). The details of imaging protocol have been described previously (17,19). In the image analysis, a three chamber view (3CV) was obtained. An auxiliary line, traversing the entire LA, was drawn perpendicular to the LV outflow tract (Figure 1). Parallel to this line, the LA APd was measured from the anterior endocardial surface to the posterior endocardial surface at the level of the aortic bulb.

The interobserver reproducibility of diametric analyses was evaluated as follows: two observers blindly and independently reconstructed the 3CV views and performed the LA APd measurements from the raw data of 21 randomly chosen subjects. Correspondingly, in the analysis of intra-observer reproducibility, one observer analyzed the above subjects twice.

LA volume was calculated from 3-mm-thick transversal slices with Simpson's method by multiplying each manually-traced LA area by the section thickness and summing-up the volumes of the separate sections (16). LA borders were traced using the mitral valve annulus as the landmark to differentiate the LA from the LV and the left atrial appendage (LAA) orifice as the landmark to differentiate the LA from the LAA (20, 21). The planimetration of the LA covered 20.0±3.2 slices. All image analyses were performed on an IDS5 diagnostic workstation (version 10.2P4; Sectra Imtec, Linköping, Sweden).

Statistical analyses. Continuous variables are presented as the mean±SD, and categorical variables as absolute values and

Table I. *Clinical characteristics of the stroke/transient ischemic attack (TIA) patients (n=146), the age- and gender-matched stroke sub-group (n=40) and control group (n=40).*

Characteristic	Main stroke/TIA group	Matched stroke/TIA sub-group	Control group	*p*-Value[a]
Age, years	60.8±10.6	53.9±9.3	53.8±9.0	ns
Males	101 (69.2%)	21 (52.5%)	21 (52.5%)	ns
Body mass index, kg/m^2	28.1±4.5	28.7±4.8	25.3±4.1	0.002
Body surface area, m^2	2.0±0.2	2.0±0.2	1.8±0.2	0.033
Caucasian	146 (100%)	40 (100.0%)	40 (100.0%)	ns
Hypertension	86 (58.9%)	16 (40.0%)	0 (0.0%)	<0.001
Dyslipidemia	60 (41.1%)	14 (35.0%)	16 (40.0%)	ns
Diabetes	22 (15.1%)	0 (0.0%)	0 (0.0%)	ns
Smokers	37 (25.3%)	16 (40.0%)	1 (2.5%)	<0.001
Left ventricular dysfunction, n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	ns
Atrial arrhythmia on 24 h Holter ECG	21 (12.3%)	0 (0.0%)	1 (2.5%)	ns
Left ventricular ejection fraction, %	62.7±10.7[b]	66.0±0.2[c]	63.7±7.7	ns
Prior myocardial infarction	18 (12.3%)	2 (5.0%)	0 (0.0%)	ns
Prior stroke/TIA	29 (19.9%)	5 (12.5%)	0 (0.0%)	0.021
Left atrial volume in cCT, ml	94.9±32.39	85.5±21.1	59.8±15.3	<0.001
Left atrial volume in cCT adjusted for height, ml/m	55.3±18.2	50.5±12.6	35.1±8.0	<0.001
Left atrial volume in cCT adjusted for BSA, ml/m^2	48.3±15.1	43.9±10.9	32.2±6.7	<0.001
Enlarged left atrial volume in CT	43 (29.5%)	20 (50.0%)	1 (2.5%)	<0.001
Left atrial anteroposterior diameter in CT, mm	39.8±7.1	37.6±5.7	30.4±5.0	<0.001
Enlarged left atrial anteroposterior diameter in CT	62 (42.5%)	19 (47.5%)	2 (5.0%)	<0.001
Left atrial anteroposterior diameter in TTE, mm	39.9±6.8	37.8±6.0	NA	NA
Enlarged left atrial anteroposterior diameter in TTE	67 (45.9%)	11 (27.5%)	NA	NA

Data are given as n (%) or mean±SD. cCT: Cardiac computed tomography; ECG: electrocardiography; NA: not assessed; ns: not significant; TEE: transesophageal echocardiogram. [a]Comparison between 40 gender- and age-matched patients and 40 controls; [b]n=145; [c]n=39.

percentages. Paired sample *t*-test was used to compare background characteristic and diametric and volumetric LA data measurements between modalities. Mann–Whitney *U*-test was used in groups without normal distributions. Chi-squared test was used for dichotomous variables. Analysis of covariance (ANCOVA) was used to control for the effects of confounding factors (hypertension and BMI) when comparing the LA volume and diameter between patients with stroke/TIA and controls. Sensitivity, specificity as well as positive and negative predictive values were calculated. Cohen's kappa (κ) test was used to elucidate the level of agreement between LA APd measurements in cCT and TTE in their abilities to detect a real LA volume enlargement. In this assessment, statistic κ <0 indicated poor agreement; 0.0-0.20, slight agreement; 0.21-0.40, fair agreement; 0.41-0.60, moderate agreement; 0.61-0.80, substantial agreement; 0.81-1.00, almost perfect agreement (22). McNemars' test was used to analyze whether the diagnostic performances of TTE and cCT differed statistically significantly. Data were analyzed using SPSS for Windows (version 19, 1989-2010; SPSS Inc., Chicago, IL, USA).

Results

Table I shows the clinical characteristics and the diametric and volumetric LA data for the patients with stroke/TIA and controls. In the pairwise comparison, patients with stroke/TIA were significantly more obese and they had a larger body surface area. In addition, there were more smokers in the stroke/TIA group. Furthermore, 40% of those in the stroke/TIA sub-group were suffering from hypertension, whereas there were no hypertensive patients in the control group.

In the comparison between age- and gender-matched pairs (n=40), both LA volume and diameter were significantly larger in the patients with stroke/TIA than in controls (volume: 85.5±21.1 ml *vs*. 59.8±15.3 ml; $p<0.001$ and diameter: 37.6±5.7 *vs*. 30.4±5.0 mm; $p<0.001$). The differences remained significant when adjusted for BMI and hypertension in ANCOVA, both separately and together ($p<0.001$ for all).

Based on volume and diametrical measurements in the control population, the upper threshold value for normal LA volume was estimated to be 90.4 ml and for normal LA APd 40.4 mm. Altogether, 43/146 (29.5%) patients displayed an enlarged LA volume. The LA APd was enlarged in 62 (42.5%) patients by cCT and in 67 (45.9%) patients by TTE. The cut-off value of 40.4 mm for LA APd by cCT had a sensitivity of 81% and specificity of 67% for the detection of LA enlargement. Correspondingly, cCT yielded a positive predictive value of 57% and a negative predictive value of 91%. In echocardiography, the diagnosis was based on conventional TTE cut-off values, with sensitivity being 65%, specificity 62%, and the positive and negative predictive values 42% and 81%, respectively. In other words, the total accuracy with LA APd by TTE was 63%, whereas it was higher with cCT, *i.e.* 76%.

According to Cohen's kappa statistics, the diametric measurements in cCT (κ=0.489, fair agreement) agreed more often with the enlarged LA volumes in volumetric assessments than diametric measurements in TTE (κ=0.234, slight agreement). The difference in diagnostic performance between modalities was statistically highly significant (p=0.002, McNemar's test for proportions).

The correlation coefficients for intra- and inter-observer reproducibility of measurements of LA APd were almost perfect (>0.924). The coefficients of variation ranged between 4.5-4.9, which indicates that there were no remarkable variations between diametrical measurements in cCT. Intra- and inter-observer reproducibility was substantial (κ>0.786) for detection of LA APd enlargement.

Discussion

The present study compared LA diameter measurements by cCT and TTE in a clinically relevant population of 146 patients with stroke. The measurement of LA diameter by cCT proved to be clinically feasible as it was relatively accurate in its ability to diagnose LA enlargement, achieving excellent reproducibility. The detailed volumetric analysis in mid-diastolic cCT in the healthy control population yielded a cut-off value of 40.4 mm for LA APd measurements, higher values were indicative of an enlarged LA. Importantly, measurements by cCT achieved higher diagnostic accuracy in their ability to detect an enlarged LA volume and were superior in this respect than the clinically widely used LA diameter measurements conducted with TTE.

In previous studies, 3D TTE was shown to underestimate LA volume by approximately 25% when cCT is used as the reference (23-25). Stolzmann *et al.* found that the diametric LA measurements from cCT images and TTE were comparable when both were imaged in ventricular end-systole (24). However, 3D echocardiography is not always available, furthermore, prospective cCT is rarely timed to the end-systolic phase.

The present study was based on a clinically-relevant setting, where cCT was conducted in mid-diastole and LA APd in TTE was measured at end-systole. Our key interest was to evaluate the diagnostic performance of the LA APd measurement in the phases where they are mainly made in average clinical practice. Mid-diastole is the most feasible cardiac cycle phase for cCT imaging since there is minimum motion artefact. It should be noted that in mid-diastole, the LA size is approximately 70-75% of its maximum, whereas the LA volume is largest at ventricular end-systole (26, 27). We found that if the LA volume increase was assessed by diametric measurements then cCT was more reliable than the widely used TTE.

TTE and cCT measurements are both clinically used estimates to elucidate LA enlargement even though they are not directly comparable since they are estimated at different phases of the cardiac cycle. It is not clear which of the phases has the highest clinical relevance. Moller *et al.* proposed that diastolic values could be more useful based on the fact that during ventricular diastole, the LA is directly exposed to left ventricular (LV) pressure through the open mitral valve (28). Accordingly, mid-diastolic volume/diametrical measurements might be more sensitive at detecting a LV diastolic dysfunction. The assessment of LA APd by cCT is a reliable means of detecting enlarged LA volume. It is also a time-saving method when there is no possibility of performing an automatized segmentation for LA volume calculation (24). Based on our non-hypertensive control population, the cut-off value for normal LA APd by cCT for both genders is 40.4 mm.

There are certain limitations to our study. Several cardiologists performed the TTE examinations as a part of their routine clinical work and, consequently, there may have been variations in the TTE technique due to wide variation in sonographic experience. TTE and cCT were usually conducted on separate days, however, the patients were hemodynamically stable and no significant change in LA diameter would be expected over the period of a few days. Thirdly, cCT imaging was carried out while the individual was holding their breath, which might have influenced the atrial size. In a recent 3D magnetic resonance imaging study, breath holding was shown to increase the minimum LA volume, whereas no difference in maximal volume was found (26).

To conclude, LA diameter measurement is a straightforward technique capable of detecting an enlarged LA volume. In this respect, diameter measurements with cCT are more sensitive and more specific than those obtained with TTE and can, therefore, be easily justified for clinical purposes. The total accuracy of cCT was clearly superior (76%) to that obtained with TTE (63%). A cut-off value of 40.4 mm for an enlarged LA can be applied to mid-diastolic measurements by cCT, such as in the commonly used coronary CTA.

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