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Assessment of the Dynamism of the Left Atrial Appendage Dimensions: A Computer Tomographic Analysis

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Abstract

Background: Device sizing prior to left atrial appendage (LAA) closure is currently primarily based on transesophageal echocardiographic as well as invasive angiographic measurements, and can be challenging due to the complex and highly variable anatomy of the LAA. Computerized tomography (CT) is a 3-dimensional imaging modality that is increasingly being used for planning structural heart disease interventions. We assessed the variability of the measurements of the LAA ostium in patients with sinus rhythm and atrial fibrillation referred for CT angiography.

Methods: 101 consecutive patients with available retrospective spiral acquisitions as well as multiphase reconstructions between 0 to 90% of the peak R-wave to R-wave were included in this analysis. All acquisitions were performed using a third generation dual source system (Somatom Force, Siemens Healthineers, Forchheim, Germany). Data sets were transferred to dedicated Software (Ziostation2, Ziosoft Inc., Tokyo, Japan) which allows dynamic evaluation of the LAA ostium through the different phases of the cardiac cycle. Multiplanar reconstructions were aligned with the plane of the LAA ostium and measurements where performed in a cross-sectional plane orthogonal to the long axis of the LAA at the level of the left circumflex coronary artery. Four measurements were performed: area, circumference, area-derived diameter (√[area/∏] x 2) and circumference-derived (perimeter/∏). Furthermore assessment of the length if the LAA was assessed in all patients.

Results: Out of 101 patients (mean age 81 ± 8 years, 61% males), 48 patients were in sinus rhythm at time of acquisition and 53 patients were in atrial fibrillation. The mean area of the LAA ostium as well as perimeter were significantly larger in AF patients compared to SR patients (464±153 vs. 359±131 mm^2 and 78±12 mm vs. 69±12 mm for AF vs SR patients, respectively, p=0.001). Consequently the area derived diameter as well as perimeter derived diameter were consequently significantly larger in AF vs. SR patients (24±4 mm vs. 21±4 mm and 25±4 vs. 22±4 mm for area-derived vs. perimeter-derived diameter, respectively, p<0.001). The percentage difference between maximal and minimal LAA dimensions were significantly higher for sinus rhythm patients compared to atrial fibrillation [88% (IQR 60; 147%) vs. 21% (IQR 13; 42%), respectively, p<0.001] for median percentage area change and 34% vs. 10% for median percentage perimeter change (IQR 25; 52 vs. 7;18%, respectively, p<0.001).
For atrial fibrillation patients, the largest LAA dimensions (area, perimeter, area-derived and perimeter-derived diameters) was measured at an average of 40% of the peak R-wave to R-wave whereas for sinus rhythm patients, the maximal LAA dimensions were measured at an average of 46% of the peak R-wave to R-wave (p>0.05). The mean length of the LAA was significantly larger in AF patients compared to SR patients (19.5 mm vs. 17 mm for AF vs SR patients, p=0.04) and the median percentage change in length was significantly higher in SR vs. AF (32% [IQR 19; 61%] vs. 13% [IQR 9; 19%] for SR vs. AF patients)

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Conclusions: Dimensions of the left atrial appendage ostium vary significantly within different time points in cardiac cycle. These changes are more pronounced in patients in sinus rhythm compared to patients in atrial fibrillation which might impact sizing if CT is used for procedural planning prior to interventional closure of the LAA. According to our data, to identify maximal LAA dimensions, CT imaging for the purpose of LAA occlusion should be targeted in atrial diastole (40-50% of the peak R-wave to R-wave).

Key Words
LAA • Closure • Sizing • CT

Introduction

The association between atrial fibrillation and ischemic cerebrovascular events has been established in numerous prospective studies [1]. Oral anticoagulation is currently the therapy of choice to prevent thromboembolic complications in patients with atrial fibrillation [2]. For patients at high risk for bleeding on anticoagulation therapy, percutaneous mechanical occlusion of the left atrial appendage (LAA) has emerged as an effective approach for stroke prevention [1]. Correct sizing is crucial for successful and safe implantation of the LAA occluder as well as for achieving desired outcomes following interventional closure. Clinically significant complications, including hemodynamically significant pericardial effusion or procedure-related stroke, are reported in up to 4% of cases [3]. Device sizing prior to left atrial appendage (LAA) closure is currently primarily based on transesophageal echocardiographic as well as invasive angiographic measurements, and can be challenging due to the complex and highly variable anatomy of the LAA. Moreover, apart from the complexity of the left atrial appendage anatomy, the LAA has the ability to contract and the dimensions of the LAA-ostium can change variably during the cardiac cycle leading to differences in sizing strategies. CT is a 3-dimensional imaging modality that is increasingly being used for planning structural heart disease interventions [4-11]. Next to its high and isotropic spatial resolution, CT has the advantage of allowing imaging throughout the entire cardiac cycle in arbitrary orientations.

Using multiphase computed tomography, we assessed the variability of the LAA dimensions in patients with sinus rhythm and atrial fibrillation throughout the cardiac cycle.

Material and Methods

Study design and patient population

This is a single center, retrospective study. Consecutive CT data sets of 101 patients referred for assessment prior to or following transcatheter aortic valve replacement were included in this analysis.

DSCT data acquisition and image reconstruction

CT data sets were acquired with a third generation dual source CT system (Somatom Force, Siemens Healthineers, Forchheim, Germany) using spiral acquisition with retrospectively ECG-gated reconstruction, with a scan range extending from the pulmonary artery bifurcation to the caudal aspect of the heart. Scan parameters were as follows: tube voltage 100 kV, tube current time product 500 mAs, collimation 2x192x0.6 mm and rotation time 250ms. ECG dose modulation was used with full radiation exposure between 10-70% of the R-wave to R-wave interval and a dose reduction to 20% outside this window. To assess contrast agent transit time, 10ml of contrast agent (Ultravist 370®, Bayer vital, Leverkusen, Germany) was used. For CT angiography, 50 ml at a flow rate of 5ml/sec, followed by a 50 ml saline chaser at the same flow rate was injected.

For each patient, a multiphase reconstruction in 10% increments of the cardiac cycle was rendered using a small field of view data set to allow for 4-dimensional assessment of the left atrial appendage. All reconstructions were rendered using a medium soft convolution kernel (Siemens Bv40) with a slice thickness of 0.75 mm and slice increment of 0.5 mm and iterative reconstruction (Admire®, Siemens Healthineers, Forchheim, Germany) at a strength level of 2.

CT analysis of left atrial appendage

For primary analysis, multiphase reconstructions were transferred to a dedicated workstation (Ziostation2, Ziosoft Inc., Tokyo, Japan). The plane of the left atrial appendage ostium was defined as a plane connecting the upper left pulmonary vein superi-

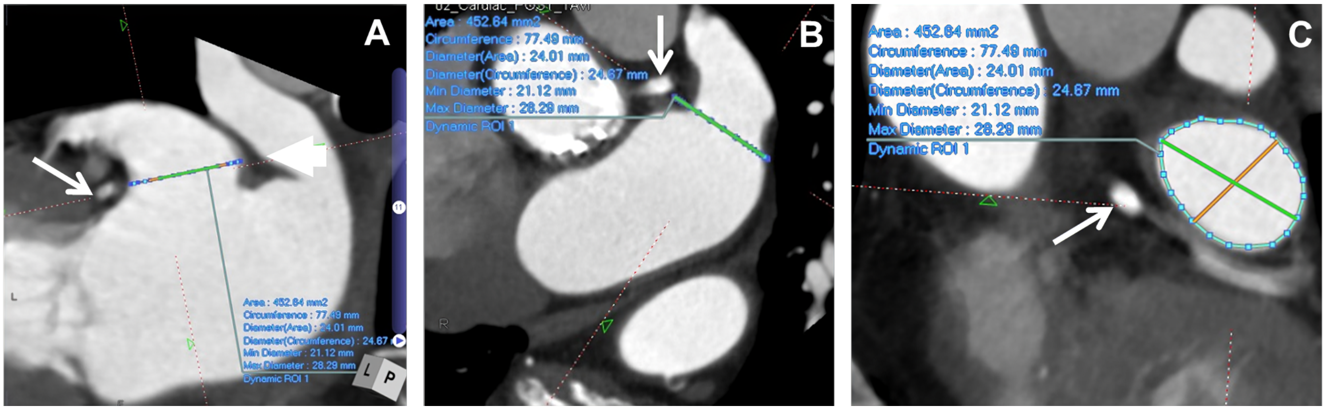

Figure 1. *Panel A & B.* Multiplanar reconstruction of the left atrial appendage (LAA) showing the plane of the ostium (**dotted line**). The plane of the ostium is orthogonal to the long axis of the LAA and extends from the upper pulmonary vein ridge (thick arrow) to the plane of the left circumflex coronary artery (**thin arrow**). *Panel C.* Tracing of the LAA ostial plane in cross-section..

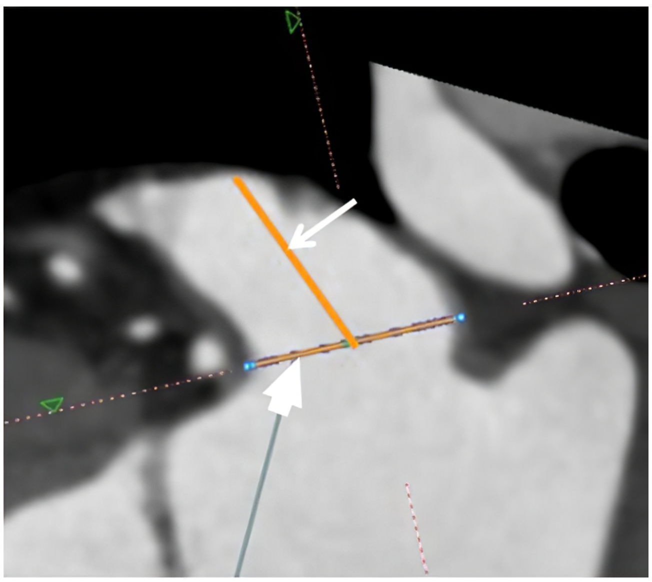

Figure 2. Multiplanar reconstruction of the left atrial appendage (LAA) showing the measurement of the length of the LAA (thin arrow). The plane of the LAA ostium is marked be the thick arrow.

orly and the connection of the left atrium and LAA inferiorly at the level of the left circumflex coronary artery. Moreover this plane was adjusted strictly orthogonal to the long axis of the LAA. The orifice of the LAA was then manually traced with at least 18 points across its contour (Figure 1) and an automated algorithm automatically provided the area, circumference, maximum and minimal diameters as well as an area-derived diameter (√[area/∏] x 2) and a circumference-derived (perimeter/∏) of the traced contour. The manual tracing of the plane of the LAA was only performed at one time point in the cardiac cycle and then automatically propagated by the software to all other phases. In every phase the tracing of the LAA ostial plane was visually verified and, if required corrected for possible errors according to the discretion of the observer. Furthermore, for each LAA the length was measured defined as the distance from the apex of the LAA to the plane of the ostium or in case of LAA with significant bends as the distance from the plane of the LAA ostium to the first bend. (Figure 2) The dimensions of the LAA ostium were compared between 48 patients with sinus rhythm and 53 in atrial fibrillation. Moreover the percentage change in dimensions (area, perimeter, area-derived diameter, perimeter derived diameter and length) defined as the percentage difference between the smallest measurement and the largest measurement were compared between both groups.

Statistical analyses

Continuous data are presented as mean ± standard deviation or median and interquartile range. Categorical variables are shown in proportions. Mean values were compared using t-test for normally distributed data and Mann-Whitney for data with non-normal distribution.

All statistical analyses were performed using IBM® (New York) SPSS® Statistics (version 21.0).

Results

Study population

101 patients were included in this analysis (mean age 81 ± 8 years, 61% males). Patients were divided in two groups: 48 patients in sinus rhythm (SR) and 53 patients in atrial fibrillation (either paroxysmal or persistent). All patients in the atrial fibrillation (AF) group were in AF during the CT acquisition. Baseline characteristics are shown in Table 1. Mean heart rate during the CT exam was 62±9 bpm for patients with sinus rhythms vs. 69±8 bpm in patients in atrial fibrillation (p=n. s).

Left atrial appendage ostium dimensions

The mean area of the LAA ostium as well as perimeter were significantly larger in AF patients compared to SR patients (464±153 vs. 359±131 mm^2 and 78±12 mm vs. 69±12 mm for AF vs SR patients, respectively, p=0.001). Consequently the area derived diameter as well as perimeter derived diameter were consequently significantly larger in AF vs. SR patients (24±4 mm vs. 21±4 mm and 25±4 vs. 22±4 mm for area-derived vs. perimeter-derived diameter, respectively, p<0.001). (Table 2 and 3) The percentage difference between maximal and minimal LAA dimensions were significantly higher for sinus rhythm patients compared to atrial fibrillation [88% (IQR 60; 147 %) vs. 21% (IQR 13; 42%), respectively, p<0.001] for median percentage area change and 34% vs. 10% for median percentage perimeter change (IQR 25;52 vs. 7;18%, respectively, p<0.001) (Figure 3).

For atrial fibrillation patients, the largest LAA dimensions (area, perimeter, area-derived and perimeter-derived diameters) was measured at an average of 40% of the peak R-wave to R-wave whereas for sinus rhythm patients, the maximal LAA dimensions were measured at an average of 46% of the peak R-wave to R-wave (p>0.05).

Left atrial appendage length

The mean length of the LAA was significantly larger in AF patients compared to SR patients (19.5 mm vs. 17 mm for AF vs SR patients, p=0.04) and the median percentage change in length was significantly higher in SR vs. AF (32% [IQR 19; 61%] vs. 13% [IQR 9;19%] for SR vs. AF patients)

Table 1: Baseline clinical characteristics.

	Sinus rhythm	AF	P-Value
Patients (n)	48	53	
Male Gender (%)	30 (62)	32 (60)	0.84
Age in years (mean ± SD)	80 ± 8	82 ± 6	0.52
Coronary artery disease (%)	28 (58)	38 (72)	0.21
Cardiovascular Risk Factors			
Dyslipidemia (%)	28 (58)	27 (51)	0.55
Hypertension (%)	36 (75)	45 (85)	0.23
Diabetes mellitus (%)	11 (23)	16 (30)	0.50
Smoking			0.74
Ex-Smoker	3(6)	4(8)	
Current Smoker	2/4)	4(8)	
Positive Family History (%)	3 (6)	4 (8)	1.00

Discussion

In this retrospective analysis, we demonstrate a significant change in LAA ostial dimensions through the cardiac cycle with maximum measurements for both perimeter as well as area measurements at 40-50% of the electrocardiographic peak R- wave to R-wave corresponding to atrial diastole. This dynamism is, as intuitively assumed more pronounced for patients in sinus rhythm – due to the contractile function of the left atrial appendage - compared to patients in atrial fibrillation (median percentage area and perimeter change 88% and 34% vs. 21% and 10% for SR vs. AF patients, respectively). Nevertheless, AF patients – a subset that might come in question for percutaneous LAA occlusion – still demonstrate a certain degree of dynamism of the LAA ostium dimensions potentially influencing sizing strategies for different LAA occluders available on market.

So far, several studies have reported on the use of 3-dimensional imaging (specifically CT imaging) prior to LAA interventions. In a large single center registry of 73 patients, Rajwani et al. reported a favorable outcome for LAA occlusion procedures using routine incorporation of CT data for pre-procedural sizing [12].

Table 2: Area measurement of LAA ostium through the cardiac cycle.

LAA Area	Sinus rhythm	AF	P-value
Mean ±SD (mm^2)	359 ± 131	464 ± 153	**0.001**
Median (mm^2)	378 ± 140	468 ± 150	**0.002**
Minimum (mm^2)	233 ± 108	406 ± 169	**< 0.001**
Maximum (mm^2)	440 ± 150	517 ± 154	**0.025**
Percentage Difference % Median (IQR)	88 (60;147)	21 (13;42)	**< 0.001**
Time point maximum area (%, R-wave to R-wave peak, mean ± SD)	46 ± 13	40 ± 15	0.16

Table 3: Perimeter measurement of LAA ostium through the cardiac cycle.

LAA Perimeter	Sinus rhythm	AF	P-value
Mean ±SD (mm)	69 ± 12	78 ± 12	**0.001**
Median (mm)	72 ± 13	79 ± 12	**0.007**
Minimum (mm, mean ± SD)	56 ± 13	73 ± 15	**< 0.001**
Maximum (mm, mean ± SD)	77 ± 13	83 ± 11	**0.031**
Percentage Difference % Median (IQR)	34 (25;52)	10 (7;18)	**< 0.001**
Time point maximum Perimeter (%, R-wave to R-wave peak, mean ± SD)	47 ± 15	41 ± 19	0.23

In their cohort - albeit in a retrospective fashion - , CT assessment altered device selection in more than half of the cases, compared to standard transoesophageal echocardiography (TEE). In this study, CT acquisitions were performed using high-pitch spiral acquisitions which per standard are set to be triggered at 60% of the peak R-wave to R-wave. However in the setting of atrial fibrillation, a clear knowledge of the exact time trigger of the acquisition remains questionable for this CT acquisition mode. Along the same line, in a cohort of 53 patients examined by Wang et al., device selection using CT imaging prior to LAA occlusion showed 100% accuracy, whereas the use of maximal LAA ostial diameters whether in 2D-TEE or 3D-TEE would have resulted in incorrect device selection in 62% and 53%, respectively [13]. In this study, sizing of the LAA was performed using ventricular systolic phases corresponding to the maximal diastolic atrial filling. In a more recent study by Eng et al., a small cohort (a total of 24 patients) was prospectively randomized to CT vs. TEE guidance prior to LAA occlusion [14]. The authors demonstrated a better device selection as well as procedural efficiency for the CT arm compared to the TEE arm. In fact, in this small cohort, the accuracy of first device selection was 92% compared to 27% for CT vs. TEE. Although CT acquisitions were performed using retrospective ECG-triggering, no clear mention of the exact time point of LAA sizing was reported. Furthermore, in a cohort of 36 patients examined using CT as well as 2-dimensional TEE, Goitein et al. reported a better prediction of device sizing prior to percutaneous LAA occlusion using perimeter assessment of LAA ostium in CT compared to diameter measurements in TEE [15]. In their cohort, acquisitions were performed in ventricular systole at 30-40% of the cardiac cycle.

Beyond 3-dimensional assessment of the LAA using CT imaging, few studies have recently reported the feasibility and usefulness of CT-based 3D printing for assessment of the LAA prior to percutaneous closure [16-18]. Using this modern technology, Hell et al. could demonstrate - in a small cohort of 22 patients treated with the Watchman® device - the additive value of CT-based 3D printing compared to anatomical CT 3-dimensional information for device selection prior to percutaneous closure [16].

Moreover, Hozawa et al. recently compared LAA volume and dimensions in 60 patients with normal sinus rhythm compared to patients with paroxysmal atrial fibrillation [19]. In their cohort, CT imaging was performed at 75% of the peak R-wave to R-wave in patients with sinus rhythm (ventricular diastolic phase) whereas for patients with paroxysmal AF, retrospective CT acquisitions along the entire cardiac cycle were available. However, for the purpose of comparison, LAA dimensions were compared only in

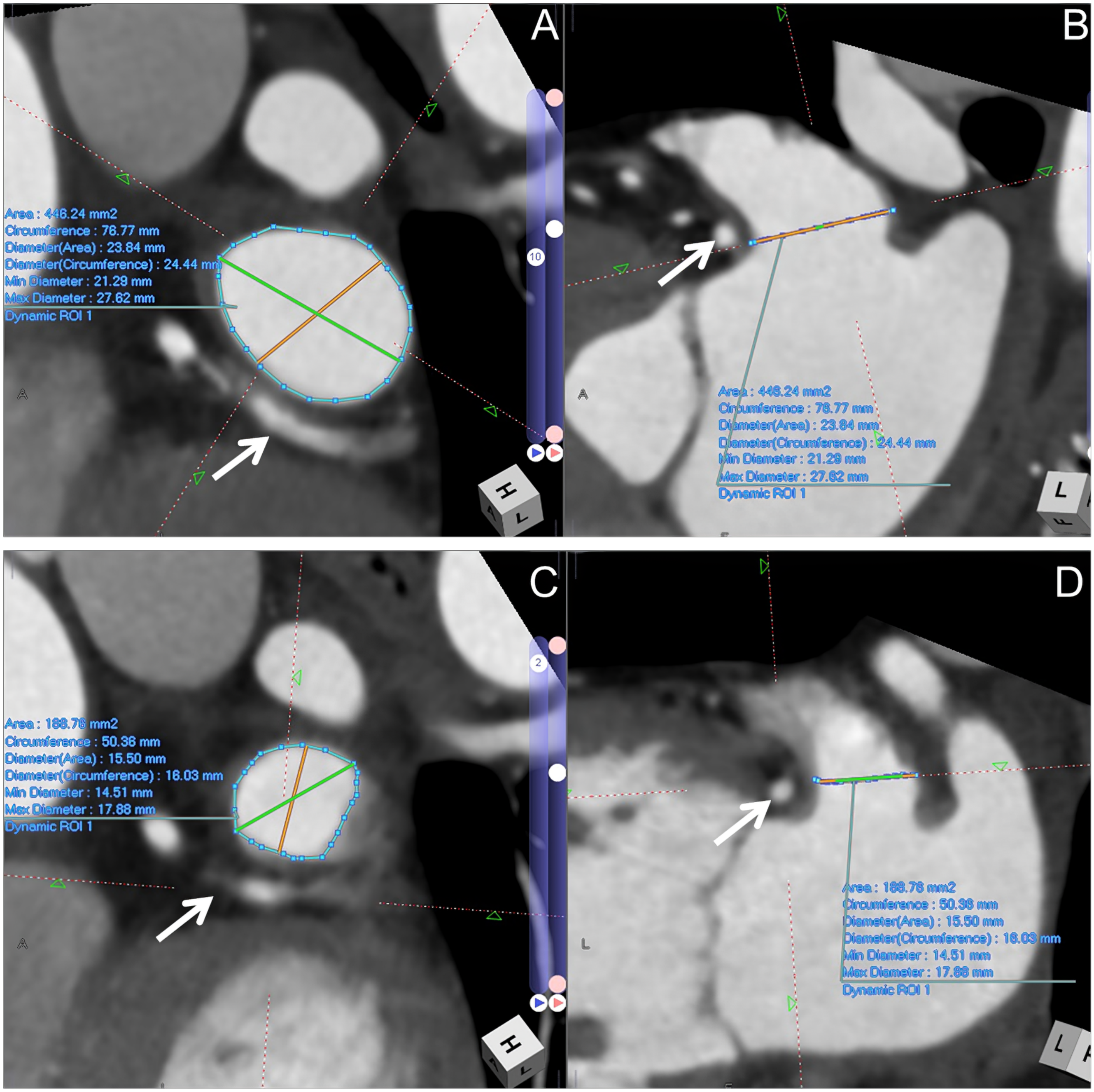

Figure 3. Computerized tomography of a 70-year-old patient in sinus rhythm. *Panels A and B* show multiplanar reconstructions of the left atrial appendage (LAA) at 45% of the peak R-wave to R-wave. *Panel A.* Tracing of the LAA ostium showing an area of 446 mm^2. *Panel B.* plane of the LAA ostium. The **arrows** mark the left circumflex coronary artery. *Panels C and D* show multiplanar reconstructions of the same patient at 5% of the peak R-wave to R-wave with significantly smaller LAA dimensions. *Panel C.* Tracing of the LAA ostium showing an area of 188 mm^2. *Panel D.* plane of the LAA ostium.

ventricular diastolic phases for both sinus rhythm and atrial fibrillation patients (75% of the peak R-wave to R-wave). Similar to our observation – albeit with comparisons only in ventricular diastolic phases- the authors report significantly larger dimensions of LAA-orifice as well as LAA volume in AF patients compared to sinus rhythm patients. Interestingly, the authors addressed a further challenging aspect of LAA assessment which is the definition of the LAA ostial plane. In their analysis, three planes were proposed for assessment of the LAA orifice. Due to the lack of anatomical boundaries between the left atrial cavity and the LAA, it still remains challenging to uniformly define the plane of the ostium. So far, the most commonly used plane for defining the LAA ostium is a plane joining the pulmonary vein ridge superiorly and the junction between the LA and the LAA inferiorly at the plane the left circumflex coronary artery. Of Interest, using a similarly defined plane in their cohort and ours, Hozawa et al. could only demonstrate a trend towards larger LAA ostial dimensions in AF patients compared to sinus rhythm, however these differences did not reach statistical significance. These differences could be probably explained by the difference in cohort size on one side, and more importantly due to the mere ventricular diastolic phase assessment in their cohort on the other side.

In light of our findings, it appears of relevant importance to plan the time of CT acquisition to the time point of maximal LAA dimensions for optimal device sizing and consequently optimal sealing of the LAA. However, we examined a cohort of patients referred for CT imaging in the context of transcatheter aortic valve replacement, as these patients were – per institutional protocol - examined using retrospective acquisition and hence multiphase assessment of LAA dimensions at different time points of the cardiac cycle was possible. In so far, whether implementing CT maximal LAA dimensions for device sizing outside this selected cohort would affect intra-procedural success as well as complications remains unclear and need to be further assessed in a prospective cohort referred for percutaneous LAA occlusion.

Several limitations in this study need to be acknowledged. First, our patient cohort included a relatively small cohort referred for CT imaging prior to transcatheter aortic valve replacement. Furthermore CT measurements were performed by a single observer once so intra- and inter-observer differences could not be reported. However, our data shed light on the importance of careful timing of CT acquisitions in the context of LAA imaging prior to interventional closure. The currently available literature is somehow heterogeneous as far as CT acquisition protocols prior to LAA occlusion are concerned. Especially with the expected increase in CT imaging in this context, standardized acquisition protocols as well as reporting algorithms need to be developed to allow for standardized reporting. According to our data, to identify maximal LAA dimensions, CT imaging for the purpose of LAA occlusion should be targeted in atrial diastole (40-50% of the peak R-wave to R-wave).

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Conflict of Interest

Mohamed Marwan has received speaker honoraria from Siemens Healthcare and Edwards Lifesciences.

Comment on this Article or Ask a Question

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