Evaluation of the Left Atrial Appendage With Real-Time 3-Dimensional Transesophageal Echocardiography
Implications for Catheter-Based Left Atrial Appendage Closure

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Background—Precise knowledge of left atrial appendage (LAA) orifice size is crucial for correct sizing of LAA closure devices. The aim of the present study was to determine the performance of real-time 3D transesophageal echocardiography (RT3DTEE) for LAA orifice size assessment, compared with 2D transesophageal echocardiography (2DTEE), and to investigate the impact of atrial fibrillation (AF) on LAA orifice size.

Methods and Results—One hundred thirty-seven patients (38 control subjects, 31 with paroxysmal AF, 38 with persistent AF and 30 with permanent AF) underwent 2DTEE and RT3DTEE. Both techniques were used to measure LAA orifice area. Clinically-indicated 64-slice computed tomography (CT) was used as reference technique in 46 patients. Two-dimensional TEE underestimated LAA orifice area, compared with RT3DTEE (1.99 ± 0.94 cm² versus 3.05 ± 1.27 cm²; \( P < 0.001 \)). RT3DTEE showed higher correlation with CT for the assessment of LAA orifice area, compared with 2DTEE (\( r = 0.92; 95\% \) confidence interval, 0.85 to 0.95, versus \( r = 0.72; 95\% \) confidence interval, 0.54 to 0.83, respectively). At Bland–Altman analysis, RT3DTEE and 2DTEE underestimated LAA orifice area, compared with CT. However, RT3DTEE showed smaller bias (0.07 cm² versus 0.72 cm²) and narrower limits of agreement (–0.71 to 0.85 cm² versus –0.58 to 2.02 cm²) with CT, compared with 2DTEE. Among AF patients, a progressive increase in RT3DTEE-derived LAA orifice area was observed with increasing frequency of AF (\( P < 0.001 \)). At multivariate analysis, AF and left atrial volume index (\( P < 0.001 \) for both) were independently associated with RT3DTEE-derived LAA orifice area.

Conclusions—RT3DTEE is more accurate than 2DTEE for the assessment of LAA orifice size. A progressive increase in LAA orifice area is observed with increasing frequency of AF. (Circ Cardiovasc Imaging. 2011;4:514-523.)

Key Words: atrial fibrillation ■ left atrial appendage ■ real-time three-dimensional transesophageal echocardiography

The left atrial appendage (LAA) is the source of thrombi in more than 90% of patients with nonvalvular atrial fibrillation (AF);–2 accordingly, removal or occlusion of the LAA may represent an effective therapeutic strategy to reduce the risk of stroke in these subjects. Previous studies have suggested the surgical exclusion of the LAA as a safe and effective procedure among AF patients undergoing open heart surgery or coronary artery bypass grafting surgery.3,4 More recently, catheter-based closure of the LAA has been proposed as a potential therapeutic approach for patients with AF ineligible or noncompliant to anticoagulation therapy; to this end, 3 devices have been specifically designed for percutaneous LAA closure and clinically tested.5–7

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Precise knowledge of LAA anatomy (and, in particular, of LAA orifice size) is crucial for correct sizing and safe placement of LAA closure devices; this information is commonly provided by 2D transesophageal echocardiography (2DTEE).8 However, 2DTEE does not adequately allow complete spatial visualization of the LAA. Consequently, three-dimensional imaging modalities, such as computed tomography (CT), cardiac magnetic resonance or real-time 3D transesophageal echocardiography (RT3DTEE), may be more appropriate.9–14 In particular, RT3DTEE may represent the first-line approach because it can provide full view of the LAA without radiation exposure and contrast administration.

Scarce data are available regarding the performance of RT3DTEE for the characterization of LAA anatomy, as compared with 2DTEE.13 In addition, unknown is the impact of presence and type (ie, paroxysmal, persistent and permanent) of AF on LAA orifice size, as assessed by RT3DTEE.

Accordingly, the aim of this study was 3-fold: first, to compare the RT3DTEE findings with those obtained with...
conventional 2DTEE; second, to evaluate the accuracy of RT3DTEE- and 2DTEE-derived measurements of LAA orifice size, using 64-slice CT as reference technique; and third, to investigate the impact of presence and type of AF on LAA dimension and particularly on LAA orifice size.

Methods

Study Population

A total of 137 consecutive patients (99 with a history of paroxysmal AF [n = 31], persistent AF [n = 38] or permanent AF [n = 30] nonvalvular AF and 38 without a history of AF) who underwent clinically indicated transthoracic and transesophageal echocardiography were prospectively included. Paroxysmal, persistent, and permanent AF were diagnosed according to the American Heart Association/American College of Cardiology/European Society of Cardiology criteria. Briefly, paroxysmal AF was defined as self-terminating episodes of AF lasting ≤7 days, whereas persistent AF was defined as episodes lasting >7 days, requiring pharmacological or electric cardioversion; patients were considered as having permanent AF when cardioversion has failed or has not been attempted.

Patients with left ventricular systolic dysfunction (left ventricular [LV] ejection [EF] fraction <50%), significant (moderate or severe) valvular heart disease, prosthetic heart valve or mitral valve repair, congenital heart disease, and technically inadequate echocardiographic studies were not included.

For each patient, the presence of coronary risk factors (systemic hypertension, hypercholesterolemia, diabetes mellitus, positive family history and cigarette smoking) and history of coronary artery disease was recorded. A history of coronary artery disease was defined as the presence of previous acute coronary syndrome,

Table 1. Baseline Characteristics of Study Population

<table>
<thead>
<tr>
<th></th>
<th>All Patients (n=137)</th>
<th>Patients Who Underwent 64-Slice CT (n=46)</th>
<th>Remaining Patients (n=91)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>68±11</td>
<td>66±11</td>
<td>69±11</td>
<td>0.23</td>
</tr>
<tr>
<td>Male sex, %</td>
<td>87 (64%)</td>
<td>31 (67%)</td>
<td>56 (62%)</td>
<td>0.50</td>
</tr>
<tr>
<td>Body surface area, m²</td>
<td>1.91±0.22</td>
<td>1.90±0.22</td>
<td>1.91±0.21</td>
<td>0.73</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>91 (66%)</td>
<td>34 (74%)</td>
<td>57 (63%)</td>
<td>0.19</td>
</tr>
<tr>
<td>Hypercholesterolemia, %</td>
<td>68 (50%)</td>
<td>30 (65%)</td>
<td>38 (42%)</td>
<td>0.009</td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td>21 (15%)</td>
<td>5 (11%)</td>
<td>16 (18%)</td>
<td>0.30</td>
</tr>
<tr>
<td>Family history of CAD, %</td>
<td>24 (18%)</td>
<td>7 (15%)</td>
<td>17 (19%)</td>
<td>0.61</td>
</tr>
<tr>
<td>Smoking, %</td>
<td>31 (23%)</td>
<td>11 (24%)</td>
<td>20 (22%)</td>
<td>0.80</td>
</tr>
<tr>
<td>CAD, %</td>
<td>42 (31%)</td>
<td>18 (39%)</td>
<td>24 (26%)</td>
<td>0.13</td>
</tr>
<tr>
<td>Atrial fibrillation, %</td>
<td>38 (28%)</td>
<td>10 (22%)</td>
<td>28 (31%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

   Absent

   Paroxysmal

   Persistent

   Permanent

   CAD indicates coronary artery disease.
calculated using the formula proposed by Devereux.17 Left atrial esophageal echocardiography (2DTEE) measurements of the left atrial appendage (LAA) orifice area versus the computed tomography (CT) reference values.

Transesophageal Echocardiography
Transesophageal echocardiography was performed using commercially available fully sampled matrix-array TEE transducer and ultrasound system (X7–2t Live 3D TEE transducer, ie33, Philips Medical Systems, Andover, MA). All images were digitally stored for offline analysis (QLAB cardiac 3DQ, Philips Medical Systems).

Two-Dimensional Transesophageal Echocardiography
Two-dimensional TEE was performed according to a standard clinical protocol.18 The LAA was imaged at 0°, 45°, 90°, and 135°. The 2D images were analyzed on-line. Measurements of maximum (D1) and minimum (D2) diameters of LAA orifice were obtained from orthogonal planes (0° and 90°, and 45° and 135°), from the origin of the left circumflex artery to the roof of the LAA, below the ligament of Marshall.8 The LAA orifice area was then calculated as previously described, using the following equation13:

\[ \text{LAA Orifice Area} = \pi \times (D1/2) \times (D2/2) \]

The larger of the 2 calculated orifice areas (on the basis of 0° and 90°, and 45° and 135°) was then chosen. An eccentricity index, measured as D1/D2 ratio, was used to assess the LAA orifice geometry. An eccentricity index = 1 would represent a perfect circle while progressively higher eccentricity index represent progressively more ellipsoid geometry. Similarly, the LAA depth (ie, the distance from LAA orifice to the tip of LAA) was measured at 0°, 90°, 45° and 135°; from these 4 views, the longest LAA depth was then chosen.13

Real-Time 3D Transesophageal Echocardiography
Acquisition of RT3DTEE images of the LAA has been previously described13; briefly, RT3DTEE imaging was performed acquiring a pyramidal data set large enough to include the entire LAA, using the zoom mode. Subsequently, pyramidal data sets were cropped along designated x-, y-, and z-axes or by using an arbitrary cropping plane, to remove remaining nonrelevent anatomic structures and to improve the visualization of LAA. The image was then rotated in order to provide an “en-face” view of the LAA (Figure 1). The 3D data sets were analyzed off-line with a dedicated software (QLab-3DQ, Philips Medical Systems), as previously described.13 The 3D data sets of the LAA were assessed using the multiplanar reconstruction (MPR) mode of QLab-3DQ software, which allows visualization and alignment of the LAA in the 3 different dimensions. The LAA long axes were aligned using MPR, allowing visualization of the LAA orifice in the short axis (Figure 1). The area of the LAA orifice, as well as the maximum (D1) and minimum (D2) diameters of LAA orifice,

### Table 2. Comparison Between 2DTEE-Derived and RT3DTEE-Derived Measurements of the LAA in the Study Population (n=137)

<table>
<thead>
<tr>
<th></th>
<th>2DTEE</th>
<th>RT3DTEE</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAA orifice area, cm²</td>
<td>1.99±0.94</td>
<td>3.05±1.27</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Maximum diameter of LAA orifice, cm</td>
<td>1.69±0.39</td>
<td>2.23±0.45</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Minimum diameter of LAA orifice, cm</td>
<td>1.43±0.37</td>
<td>1.65±0.43</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Eccentricity index of LAA orifice</td>
<td>1.21±0.19</td>
<td>1.36±0.27</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Depth of LAA, cm</td>
<td>2.67±0.77</td>
<td>2.82±0.79</td>
<td>0.001</td>
</tr>
</tbody>
</table>

2DTEE indicates 2-dimensional transesophageal echocardiography; LAA, left atrial appendage; RT3DTEE, real-time 3-dimensional transesophageal echocardiography.
were measured from the short-axis view, along a plane connecting the origin of the left circumflex artery to the roof of the LAA, below the ligament of Marshall.8 An eccentricity index of the LAA orifice was measured as previously described for 2DTEE. The LAA depth (ie, the longest distance from LAA orifice to the tip of LAA) was measured from the long-axes views. All 2D and 3D measurements of LAA were performed at ventricular end-systole. In patients who were in AF at the time of transthoracic and transesophageal echocardiography, measurements from ≥3 cardiac cycles were averaged.

Sixty-Four–Slice Computed Tomography
A subset of 46 patients (10 control patients, 20 patients with paroxysmal AF, and 16 patients with persistent AF) underwent also clinically indicated 64-slice CT (LightSpeed VCT, GE Healthcare, Milwaukee, WI) within 1 month of transthoracic and transesophageal echocardiography. All patients were in sinus rhythm during the CT scan. A retrospective ECG-gating protocol was used. Scanning parameters were the following: detector collimation of 0.625 mm, total z-axis coverage of 40 mm per rotation, gantry rotation speed of 0.35 seconds, tube voltage of 120 kV, a pitch of 0.16 to 0.24, and ECG modulated tube current ranging from 400 mA to 800 mA. The bolus tracking technique (SmartPrep) was used to trigger the acquisition, with a four-cavity view as the region of interest. A total of 70 to 100 mL of iodinated, nonionic contrast agent (Optiray 350, Mallinckrodt, St Louis, MO) was injected continuously into the antecubital vein (80 to 100 mL at 5.0 mL/s), followed by a 30-mL saline flush.
injected at a flow rate of 3.0 mL/s. Scanning was initiated during a single breath hold for an acquisition time of 5 to 7 seconds. All images were reconstructed with an effective slice thickness of 0.625 mm. ECG-gating protocol reconstruction of the image data were performed starting from early systole (10% of R-R interval) and ending at end-diastole (90% of R-R interval) using 10% steps. Reconstructed image data were transferred to a remote workstation (Advantage Windows 4.3, GE Healthcare) for postprocessing. For the purpose of the current study, image data sets reconstructed at end-systole (40% of R-R interval) were used for analysis. Using MPR, measurements of the area of the LAA orifice were performed from the short-axis view as well as the maximum (D1) and minimum (D2) diameters of LAA orifice. An eccentricity index of LAA orifice was measured as previously described for RT3DTEE and 2DTEE. The LAA depth (ie, the longest distance from LAA orifice to the tip of LAA) was measured from the long-axes views.

To avoid measurements bias, all analyses were performed in blinded fashion by different operators.

**Statistical Analysis**

Continuous variables are expressed as mean and standard deviation. Categorical data are presented as absolute numbers and percentages. Differences in continuous variables between 2 groups were assessed using Student t test or Mann-Whitney U test, if appropriate. Differences in continuous variables between more than 2 groups were assessed using the 1-way ANOVA test or the Kruskal-Wallis test, when appropriate; if the result of analysis was significant, post hoc test with Bonferroni correction was applied. \( \chi^2 \) test or Fisher exact test, when appropriate, was computed to assess differences in categorical variables.

The measurements of the LAA (ie, LAA orifice area, maximum and minimum diameters of LAA orifice, eccentricity index of the LAA orifice area, and LAA depth) were compared between RT3DTEE and 2DTEE with the paired t test. Correlation between RT3DTEE- and 2DTEE-derived LAA orifice areas with CT-derived LAA orifice area was summarized using linear regression analysis and Pearson correlation coefficients. The method of Bland and Altman was used for agreement analysis between RT3DTEE,
2DTEE, and CT-derived measurements of LAA orifice area. Concordance correlation coefficient (CCC) was evaluated to assess intra- and interobserver reproducibility of CT, RT3DTEE, and 2DTEE-derived measurement of LAA orifice area, repeating the analysis 1 month later by the same observer who performed the first analysis and by a second independent observer.

Univariate and multivariate linear regression analyses (enter method) were performed to evaluate the relationship between LAA orifice area (measured with RT3DTEE) and the following variables: age, male sex, body surface area, AF, coronary risk factors, coronary artery disease, LVEDV index, LVESV index, LVEF, LV mass index, and LAV index. Only significant variables at univariate analysis were entered as covariates in the multivariable model.

A 2-tailed probability value $<0.05$ was considered statistically significant. Statistical analysis was performed using the SPSS (SPSS 15.0, Chicago, IL) and MedCalc (MedCalc 10.0, Mariakerke, Belgium) software packages.

Results

Baseline Characteristics of the Study Population

Baseline characteristics of the study population are shown in Table 1. The acquisition of 2DTEE and RT3DTEE images was possible in all patients without complications. In particular, as regard to RT3DTEE, the LAA was always completely imaged within the 3D dataset, enabling a 100% feasibility of LAA assessment.

Comparison Between RT3DTEE, 2DTEE, and CT

As shown in Table 2, 2DTEE provided significant lower measurements of LAA orifice area, maximum and minimum diameter of LAA orifice, eccentricity index of LAA orifice and depth of LAA, as compared with RT3DTEE.

By linear regression analysis (Figure 2), RT3DTEE showed better correlation with CT in the assessment of LAA orifice area, compared with 2DTEE ($r^{2} = 0.92$, $95\%$ confidence interval [CI], $0.85$ to $0.95$, versus $r^{2} = 0.72$, $95\%$ CI, $0.54$ to $0.83$, respectively). At Bland-Altman analysis (Figure 3), both RT3DTEE and 2DTEE underestimated the LAA orifice area, as compared with CT. However, RT3DTEE showed smaller bias and narrower limits of agreement with CT, as compared with 2DTEE (Figure 3). Intraobserver and interobserver reproducibility of CT-derived measurement of LAA orifice area was good (CCC = 0.97 [95% CI, 0.96 to 0.99] and = 0.96 [95% CI, 0.94 to 0.98], respectively). Intraobserver and interobserver reproducibility of RT3DTEE-derived measurement of LAA orifice area was also good (CCC = 0.97 [95% CI, 0.95 to 0.98] and = 0.94 [95% CI, 0.90 to 0.97], respectively).
respectively) and better than that observed for 2DTEE (CCC=0.92 [95% CI, 0.86 to 0.95] and =0.88 [95% CI, 0.79 to 0.93], respectively).

Relation Between AF and LAA Dimension
Baseline and 2DTE characteristics of each group are shown in Table 3. No significant differences among groups were observed for most of the baseline clinical characteristics. Similarly, no significant differences among groups were observed in LV volumes, LVEF and LV mass.

No significant difference in LAV index was observed between control patients and patients with history of paroxysmal AF; conversely, a progressive increase in LAV index was observed with increasing frequency of AF (Table 3).

As shown in Figure 4, no significant difference in LAA orifice area, maximum and minimum diameter of LAA orifice, eccentricity index of LAA orifice, and depth of LAA was observed between control patients and patients with history of paroxysmal AF. Conversely, a progressive increase in LAA dimension (ie, LAA orifice area, maximum and minimum diameter of LAA orifice, and depth of LAA) and a progressive reduction of eccentricity index of LAA orifice were observed with increasing frequency of AF (Figure 4).

Determinants of LAA Orifice Area
Table 4 shows the results of univariate and multivariate linear regression analysis performed to determine the factors related to LAA orifice area in the study population. At univariate analysis, several variables were significantly related to LAA orifice area: age, AF, hypertension, diabetes mellitus, and LAV index. However, at multivariate analysis, only AF and LAV index (P<0.001 for both) were independently associated with LAA orifice area.

Discussion
The results of the present study can be summarized as follows: (1) RT3DTEE-derived measurements of LAA orifice area are closely related with CT measurements, which is the gold standard for LAA anatomic evaluation; (2) 2DTEE significantly underestimates LAA dimension and orifice size, as compared with RT3DTEE; (3) a progressive increase in LAA dimension and a progressive reduction of eccentricity index of LAA orifice are observed with increasing frequency (ie, from paroxysmal to permanent form) of AF episodes; and (4) AF, as well as LAV index, are independently related to LAA orifice area.

Imaging Techniques for LAA Orifice Size Assessment
Precise knowledge of LAA orifice dimension is crucial for correct sizing and safe placement of LAA closure device; usually, the size of the device is chosen few millimeters larger than the diameter of the LAA orifice (Table 5), to ensure sufficient and stable positioning of the device itself.8,19 Even though device migration, dislodgment, or embolization, cardiac perforation and pericardial effusion are rarely described, especially when the procedure is performed by experienced operators, significant oversizing or undersizing of the device may potentially increase the risk of such complications.20–22

Commonly, assessment of LAA orifice size is performed using 2DTEE; however, 2DTEE has some limitations, which are inherent to its 2D nature. When using 2DTEE, measurements must be performed in multiple views and foreshortening and limited echo planes may potentially lead to imperfect estimation of LAA orifice size, as shown by the results of the present study. Three-dimensional imaging modalities, such as CT, cardiac magnetic resonance, and RT3DTEE, should therefore be preferred.9–14 However, CT is associated to non-negligible radiation exposure, whereas cardiac magnetic resonance is expensive and not widely available. In addition, both these techniques cannot be performed at bedside and do not provide real-time images of the LAA. Thus, RT3DTEE

Table 4. Univariate and Multivariate Regression Analyses to Determine the Independent Correlates of LAA Orifice Area in the Study Population

<table>
<thead>
<tr>
<th></th>
<th>Univariate Analysis</th>
<th>Multivariate Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>β</td>
<td>P Value</td>
</tr>
<tr>
<td>Age</td>
<td>0.20</td>
<td>0.022</td>
</tr>
<tr>
<td>Male sex</td>
<td>−0.016</td>
<td>0.85</td>
</tr>
<tr>
<td>Body surface area</td>
<td>0.059</td>
<td>0.49</td>
</tr>
<tr>
<td>AF*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paroxysmal</td>
<td>−0.055</td>
<td>0.11</td>
</tr>
<tr>
<td>Persistent</td>
<td>0.56</td>
<td>0.16</td>
</tr>
<tr>
<td>Permanent</td>
<td>0.78</td>
<td>0.46</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.21</td>
<td>0.013</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>−0.11</td>
<td>0.18</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0.35</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Family history of CAD</td>
<td>−0.005</td>
<td>0.96</td>
</tr>
<tr>
<td>Smoke</td>
<td>−0.076</td>
<td>0.38</td>
</tr>
<tr>
<td>CAD</td>
<td>−0.021</td>
<td>0.81</td>
</tr>
<tr>
<td>LV EDV index</td>
<td>0.10</td>
<td>0.24</td>
</tr>
<tr>
<td>LV ESV index</td>
<td>0.097</td>
<td>0.26</td>
</tr>
<tr>
<td>LV EF</td>
<td>−0.017</td>
<td>0.85</td>
</tr>
<tr>
<td>LV mass index</td>
<td>0.074</td>
<td>0.39</td>
</tr>
<tr>
<td>LAV index</td>
<td>0.70</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

LAA indicates left atrial appendage; AF, atrial fibrillation; CAD, coronary artery disease; LV, left ventricular; EDV, end-diastolic volume; EF, ejection fraction; ESV, end-systolic volume; and LAV, left atrial volume.

*AF was entered as a categorical variable, with 4 possible levels (ie, 0=no AF; 1=paroxysmal AF; 2=persistent AF; and 3=permanent AF). Three degrees of freedom test was used.

or undersizing of the device may potentially increase the risk of such complications.20–22

Table 5. Size of LAA Closure Devices and Maximum Diameter of LAA Orifice Recommended for Device Implantation

<table>
<thead>
<tr>
<th>Device</th>
<th>Device Size</th>
<th>Recommended Maximum Diameter of LAA Orifice</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLATO</td>
<td>20–32 mm</td>
<td>13.6–26.5 mm</td>
</tr>
<tr>
<td>WATCHMANN</td>
<td>21–33 mm</td>
<td>17–31.9 mm</td>
</tr>
<tr>
<td>Amplatz Cardiac Plug</td>
<td>16–30 mm</td>
<td>12.6–28.5 mm</td>
</tr>
</tbody>
</table>

LAA indicates left atrial appendage.
From References 8 and 19,8,19
may represent the first-line approach, due to its ability to provide real-time 3-dimensional en face views of the LAA without radiation exposure and contrast administration.

In the present study, 2DTEE-derived measurements of LAA dimension were compared with those obtained with RT3DTEE; in addition, the accuracy of RT3DTEE- and 2DTEE-derived measurements of LAA orifice size was assessed, using 64-slice CT as reference technique. Importantly, all the patients had adequate RT3DTEE images for visualization and quantitation of the LAA, confirming the good feasibility previously reported by other groups. Of note, 2DTEE significantly underestimated LAA dimensions, as compared with RT3DTEE. Importantly, RT3DTEE was significantly more accurate and reproducible than 2DTEE in the measurement of LAA orifice size, probably because RT3DTEE, by using the MPR mode, allows correct identification and direct planimetric measurement of the LAA orifice area. Conversely, 2DTEE estimates the LAA orifice area using the equation: LAA orifice area = \( \pi \times (D1/2) \times (D2/2) \). Consequently, small errors in the measurements of the diameters can be amplified, therefore reducing accuracy and reproducibility.

These results are in line with those previously described in a smaller study population by Shah et al and have relevant clinical implications. On the basis of 2DTEE-derived measurement of LAA orifice size, LAA occlusion device may be frequently undersized; early clinical experience of LAA occlusion have indeed shown that the size of the device correctly matching the size of the LAA orifice is often 20% to 40% larger than predicted by 2DTEE. This obviously exposes the patient to the need of intraoperative device resizing and to potential complications. In addition, patients not suitable for LAA occlusion because of too-large LAA may inappropriately be referred to device implantation; in the present study, indeed, according to the size of LAA closure devices and to the maximum diameter of LAA orifice recommended for device implantation (Table 5), all patients would be considered suitable for device implantation on the basis of 2DTEE measurements. Conversely, on the basis of RT3DTEE measurements, 26 (19%) patients (1 with paroxysmal AF, 11 with persistent AF and 14 with permanent AF) would not be suitable for PLAAOT device implantation, 5 (4%) patients (all of whom with permanent AF) would not be suitable for WATCHMANN LAA system implantation and 15 (11%) patients (9 with persistent AF and 6 with permanent AF) would not be suitable for Amplatzer Cardiac Plug implantation.

Impact of Presence and Type of AF on LAA Dimension

Prior studies have demonstrated that LA dimension, function and wall fibrosis are strictly related to the AF burden. Conversely, few data are available regarding the impact of AF on the dimension and morphology of LAA orifice. According to previous postmortem studies, AF patients have a significantly larger LAA, compared with patients with normal sinus rhythm; in addition, these studies have shown that the shape of the LAA orifice is elliptical rather than round. The present study extends these previous observations, providing meaningful information on the impact of clinical and structural variables on LAA orifice area. A progressive increase in LAA dimension was indeed observed with increasing frequency of AF. Importantly, AF, as well as LAV index, was independently associated with LAA orifice area, possibly reflecting a stretch of the LAA orifice in an enlarged LA, which is frequently observed in AF patients. Of note, the progressive increase in LAA dimension with increasing frequency of AF was associated with a progressive decrease in its eccentricity index (which means that the LAA orifice was progressively less elliptical and more round-shape). These findings have significant clinical implications. On the basis of presupposed anatomic LAA maximum diameter requirements (Table 5), as shown above, most of paroxysmal AF patients would qualify for percutaneous LAA closure; however, taking into account that all the available occluders have a round shape, a round implant over an oval-shaped orifice (usually observed in this subgroup of AF patients) may lead to incomplete sealing of the orifice and to residual leaks. The clinical significance of residual leaks after device implantation is still questioned. It has been postulated that residual leaks may be a risk for thrombi formation and embolic events in patients with partially occluded LAAs, therefore leading to the need of continued anticoagulation therapy. This suggests that among AF patients with non-dilated and elliptical LAA orifice, devices may need to be elliptical to adequately occlude the LAA orifice.

On the other side, as shown above, a nonnegligible proportion of patients with persistent or permanent AF would not qualify for percutaneous LAA closure, due to an oversized LAA orifice. Of note, Beinart et al recently demonstrated, by using magnetic resonance angiography, larger LAA dimensions in AF patients with history of stroke and transient ischemic attack as compared with patients without history of embolic events. In addition, after adjustment for traditional stroke risk factors, LAA dimension emerged as an independent and powerful predictor of stroke and transient ischemic attack in AF patients; the authors explain this finding hypothesizing that larger LAAs probably are more prone to low blood flow, blood stasis, and therefore to thrombus formation. Consequently, and according to the results of the present study, many of the AF patients who may benefit more from percutaneous LAA closure would not be suitable for the procedure; this has important engineering implications for the future development of larger LAA closure devices.

Conclusions

RT3DTEE is more accurate than 2DTEE for the assessment of LAA orifice size; accordingly, RT3DTEE should be preferred for the correct sizing of LAA closure devices. Of note, LAA orifice becomes larger and more round-shaped with increasing frequency of AF; this indicates that devices with multiple sizes and shapes may be needed to ensure an adequate LAA occlusion in all AF patients.
Accordingly, further technological improvement to ensure complete LAA sealing and to prevent device leak because of shape or eccentricity issues appears to be required.

Disclosures

None.

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CLINICAL PERSPECTIVE

Precise knowledge of left atrial appendage (LAA) orifice size is crucial for correct sizing of LAA closure devices. Commonly, assessment of LAA orifice size is performed using 2D transesophageal echocardiography (2DTEE); however, 2DTEE has some limitations, inherent to its 2D nature. In the present study, the performance of real-time 3D transesophageal echocardiography (RT3DTEE) for LAA orifice size assessment, compared with 2DTEE, was evaluated and the impact of atrial fibrillation (AF) on LAA orifice size was investigated. As compared with computed tomography, which was used as reference technique, RT3DTEE was found to be more accurate than 2DTEE for the assessment of LAA orifice size. Accordingly, RT3DTEE should be preferred to 2DTEE for the sizing of LAA closure devices. Regarding the impact of AF on LAA orifice, LAA orifice has been observed to be oval-shaped in control subjects and paroxysmal AF patients and to become larger and more round-shaped with increasing frequency of AF (ie, from paroxysmal to permanent form). Considering that all available occluders have a round shape, a round implant over an oval-shaped orifice (usually observed in paroxysmal AF patients) may lead to incomplete sealing of the orifice and to residual leaks. In addition, on the basis of the prespecified anatomic LAA requirements of available occluders, some persistent or permanent AF patients may not qualify for percutaneous LAA closure, due to an oversized LAA orifice. These observations suggest that further technological improvement is needed to ensure complete LAA sealing and to prevent device leak because of shape or eccentricity issues.
Evaluation of the Left Atrial Appendage With Real-Time 3-Dimensional Transesophageal Echocardiography: Implications for Catheter-Based Left Atrial Appendage Closure
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