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Two-dimensional versus three-dimensional transesophageal echocardiography in percutaneous left atrial appendage occlusion

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Abstract

Background: *Real-time three-dimensional transesophageal echocardiography (RT3D TEE) enables better visualization of the left atrial appendage (LAA) and may be superior to real-time two-dimensional transesophageal echocardiography (RT2D TEE) for LAA occlusion (LAAO). The aim of this study was to assess inter- and intra-observer variability of RT2D TEE and RT3D TEE measurements of LAA, and to assess the accordance of RT2D TEE and RT3D TEE with appropriate occluder selection.*

Methods: *Transesophageal echocardiography was performed in 40 patients during LAAO. RT2D TEE and RT3D TEE measurements of the ostium and landing zone were performed independently by two echocardiographers. The appropriate choice of occluder was confirmed with fluoroscopic criteria. After the procedures, RT2D TEE and RT3D TEE evaluation were repeated separately by the same echocardiographers.*

Results: *The mean ostium diameters by RT2D TEE obtained by the two observers were 23.6 ± 4.2 vs. 24.8 ± 5.2 ($p = 0.04$), and the mean landing zone diameters were 17.7 ± 4.4 vs. 19.4 ± 3.9 ($p < 0.01$). In the case of RT3D TEE, the ostium diameters were 29.6 ± 5.3 vs. 29.4 ± 6.4 (p = not significant [NS]) and the landing zone diameters were 21.4 ± 3.8 vs. 21.6 ± 3.9 (p = NS). Intra-observer differences were absent in the case of RT3D TEE. The comparison of RT2D TEE vs. RT3D TEE analyses performed by the same echocardiographer revealed significant differences in the ostium and landing zone measurements (both $p < 0.01$). Agreement between the suggested device size was better for RT3D TEE (weighted kappa was 0.62 vs. 0.28, respectively).*

Conclusions: *The results obtained with RT3D TEE showed significantly larger dimensions of the ostium and the landing zone. RT3D TEE showed lesser inter- and intra-observer variability and better agreement with the implanted device.* (Cardiol J 2019; 26, 6: 687–695)

Key words: left atrial appendage occlusion, real-time two- and three-dimensional transesophageal echocardiography, Amplatzer Occluder

Introduction

Atrial fibrillation (AF) is the most common arrhythmia worldwide and its prevalence is estimated to increase further because of population ageing [1]. The most dangerous complication of AF is ischemic cerebral stroke (ICS). Although oral anticoagulants (OAC) have proven to be effective in preventing ICS [2–4], its risk still remains high in AF patients [5]. In many patients, treatment with OAC may be contraindicated or risky because of conditions such as recurrent bleeding, low compliance, or drug

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intolerance. Left atrial appendage (LAA) occlusion (LAAO) may be considered as an alternative method for ICS prevention [6–8]. According to the guidelines of the European Society of Cardiology, LAAO may be considered in AF patients with high risk of ischemic stroke and contraindications for long-term oral anticoagulation [9].

The technical and clinical success of LAAO depends on correct assessment of the ostium and the landing zone dimensions [10]. Selection of the optimal occluder size remains a challenge as each of the available imaging modalities have some limitations. The main methods of LAA imaging are: conventional cardiac angiography (CCA), transesophageal echocardiography (TEE), and cardiac computed tomography (CCT) angiography [11]. Recent data shows that CCT facilitates a more adequate occluder selection than real-time two-dimensional transesophageal echocardiography (RT2D TEE), and reduces the risk of high-flow leaks and device malposition because of under sizing [12]. However, it is costly, requires injection of a contrast medium, and is not useful for guiding the procedure. Some analyses performed for aortic valve evaluation showed that real-time three-dimensional transesophageal echocardiography (RT3D TEE) may provide more accurate assessment and its results are better correlated with CCT than RT2D TEE [13]. Till date no inter- or intra-observer studies comparing RT2D TEE and RT3D TEE in LAAO procedures have been conducted.

Thus, the aim of this study was to compare RT2D TEE and RT3D TEE in LAAO performed by two independent echocardiographers to determine which method gives more reproducible results and facilitates the selection of the optimal occluder size.

Methods

Left atrial appendage occlusion was performed in 40 consecutive patients with both paroxysmal or persistent/permanent AF (mean age 70 ± 8 years; male 57%) of which 14 were in sinus rhythm during the procedure. In line with the current recommendations, all patients had indications for ICS prevention based on the CHA_2DS_2-VASc score (mean 4.2 ± 1.5). Selection of patients was based on the EHRA/EAPCI expert consensus statement, which included: the presence of contraindications to OAC (e.g. thrombocytopenia, cancer), irreversibly high risk of bleeding according to the HAS-BLED score, and the presence of ICS despite OAC treatment [14]. The mean HAS-BLED score was 3.3 ± 0.9.

Table 1. Group characteristics.

Age [years]	70 ± 8
Male [n]	57% [23]
HAS-BLED score	3.3 ± 0.9
CHA_2DS_2-VASc score	4.2 ± 1.5
Hypertension [n]	82% [33]
Diabetes [n]	37% [37]
Coronary heart disease [n]	75% [30]
Paroxysmal atrial fibrillation [n]	47% [19]

Patients with a LAA thrombus, LAA dimension being too small or too large for LAAO, LAA depth < 10 mm, or an elongated shape of the ostium did not qualify for the procedure. Clinical characteristics of the study population are presented in Table 1.

LAAO procedure

The LAAO procedure was performed under general anesthesia. Access to the right atrium was obtained via the femoral vein. A transseptal puncture was performed to reach the left atrium. Heparin was subsequently administered to obtain activated clotting time above 250 s. After the introduction of a pig-tail catheter to the LAA, CCA of the LAA was performed. The LAA was visualized from different views to find the largest diameter of the LAA neck. The procedures were guided by both fluoroscopy and transesophageal echocardiography.

Transesophageal echocardiography

Electrocardiographic (ECG) gated transesophageal echocardiography was performed using Vivid E9 (6 VT-D probe; 5 MHz). On the day before LAAO, a pre-procedural TEE screening was performed to assess the LAA morphology, exclude an LAA thrombus, and verify the compatibility of the LAA neck dimension with the occluder size.

The ostium, neck, and body of the LAA were visualized in different views. In case of RT2D TEE images, views obtained at ~45°, 90°, and 135° were analyzed. The left circumflex artery was visualized in each case as a reference point for detection of the landing zone. Three measurements were obtained: dimension of the ostium (the line between the left lateral ridge and the ridge separating the LAA from the mitral valve), dimension of the landing zone (starting approximately 10 mm from the left lateral ridge inside the LAA to a point located approximately 5 mm below the circumflex artery), and the depth of the LAA neck (an orthogonal line from the middle of the orifice into the back wall of the LAA).

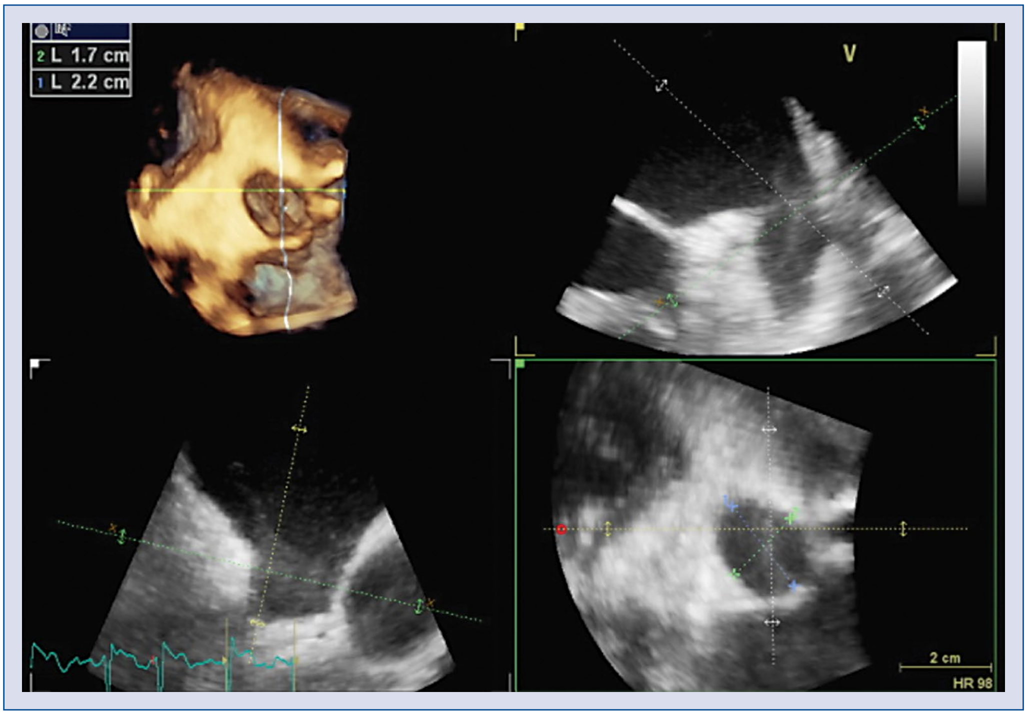

Figure 1. An example of flexi-slice real-time three-dimensional transesophageal echocardiography left atrial appendage image analysis for the measurement of the landing zone dimension.

RT3D TEE zoom images were obtained from one ECG cycle. Gain was adjusted to eliminate artefacts but not to allow for drop-out effect. The ostium and landing zone dimensions were measured in three perpendicular planes using the flexi-slice technique. The ostium level was measured between the pulmonary ridge and the tissue located between the mitral valve and circumflex artery. The landing zone level was assessed approximately 10 mm below the ostium. The largest diameter of LAA ostium was used as a reference for the selection of the occluder size (Fig. 1).

All images were stored on a disk and after the procedure, two independent echocardiographers evaluated the RT2D TEE and RT3D TEE images for ostium and landing zone measurements. The dimensions of LAA ostium and landing zone were assessed twice by each echocardiographer on two different occasions to determine the method with more reproducible results. Based on the two results of LAA landing zone dimensions and the manufacturer sizing chart, retrospectively the best occluder size was selected. The obtained results were then compared with the actual size of the implanted devices.

Occluder sizing

The Amplatzer Cardiac Plug or Amplatzer AMULET (St. Jude Medical, Minneapolis, MN, USA) were used for LAA closure. CCA was used as a referential method for occluder sizing under the condition that the difference with intraprocedural RT2D TEE or RT3D TEE measurement could not be more than 2 mm. If the difference was above 2 mm then measurements were repeated. The size of the device was selected depending on the landing zone dimension, according to the manufacturer sizing chart.

The post-procedural results were assessed with fluoroscopy and transesophageal echocardiography. The criteria for optimal implantation were: separation between the device lobe and the disc, "tire-shaped" lobe, concave-shaped disc, axis of the device lobe parallel to the LAA neck axis, and > 2/3 of the lobe past the circumflex artery.

Statistical analysis

The quantitative data was presented as mean ± standard deviation (SD). Inter- and intra-observer variability was analyzed with Student's t-test for dependent samples. The Bland-Altman plot with multiple measurements per subject was used to assess whether RT2D TEE and RT3D TEE may be used interchangeably. The agreement of RT2D TEE and RT3D TEE with the implanted device was calculated with weighted kappa statistics.

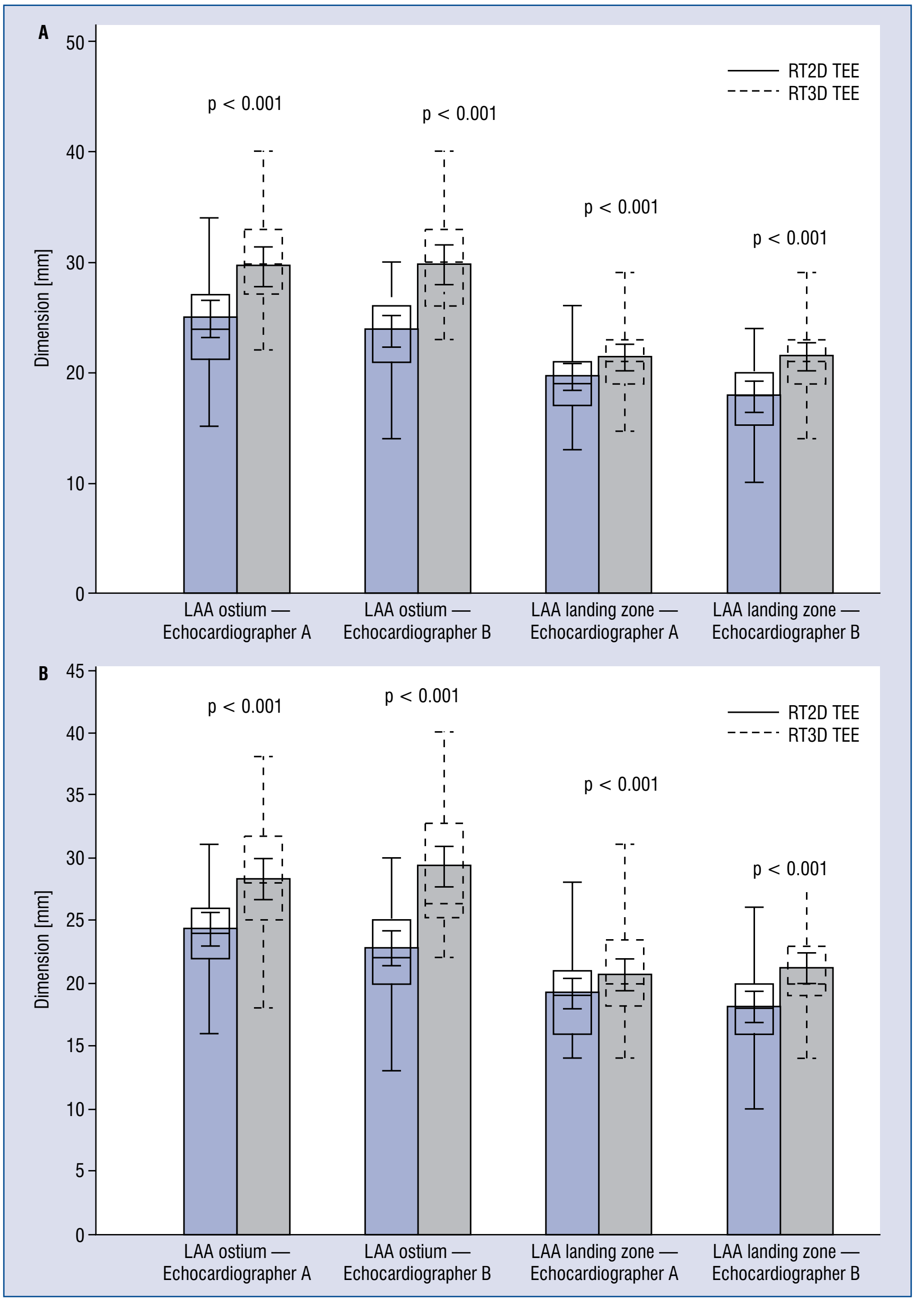

Figure 2. Comparison of real-time two-dimensional transesophageal echocardiography (RT2D TEE) versus real-time three-dimensional transesophageal echocardiography (RT3D TEE) results of left atrial appendage (LAA) ostium and LAA landing zone measurement; **A.** Primary analysis; **B.** Reaanalysis.

Results

The mean ostium diameters by RT2D TEE measurements obtained by the two observers were 23.6 ± 4.2 vs. 24.8 ± 5.2 ($p = 0.04$), and the mean landing zone diameters were 17.7 ± 4.4 vs. 19.4 ± 3.9 ($p < 0.01$). In the case of RT3D TEE, the mean ostium diameters were 29.6 ± 5.3 vs. 29.4 ± 6.4 (p = not significant [NS]) and the landing zone diameters were 21.4 ± 3.8 vs. 21.6 ± 3.9 (p = NS). Both the first and repeated measurements of the LAA landing zone and ostium obtained with RT2D TEE were lower than those obtained with RT3D TEE (Fig. 2A, B). The differences were statistically significant.

Analysis of the RT2D TEE data obtained by the two echocardiographers showed significant differences, both with regard to the LAA ostium and the LAA landing zone assessment (both smaller when measured by echocardiographer A). Similar results

Table 2. Inter-observer variability for RT2D TEE and RT3D TEE.

Diameter	Echocardiographer A	Echocardiographer B	P
Primary analysis			
Ostium (RT2D TEE) [mm]	24.8 ± 5.2	23.6 ± 4.2	0.04
Landing zone (RT2D TEE) [mm]	19.4 ± 3.9	17.7 ± 4.4	< 0.01
Ostium (RT3D TEE) [mm]	29.4 ± 6.4	29.6 ± 5.3	NS
Landing zone (RT3D TEE) [mm]	21.6 ± 3.9	21.4 ± 3.8	NS
Repeated analysis			
Ostium (RT2D TEE) [mm]	22.8 ± 4.2	24.3 ± 4.3	< 0.01
Landing zone (RT2D TEE) [mm]	18,1 ± 3.7	19.2 ± 3.6	< 0.01
Ostium (RT3D TEE) [mm]	28.6 ± 5.2	29.3 ± 5.0	NS
Landing zone (RT3D TEE) [mm]	21.2 ± 3.7	20.7 ± 3.8	NS

RT2D TEE — real time two-dimensional transesophageal echocardiography; RT3D TEE — real time three-dimensional transesophageal echocardiography

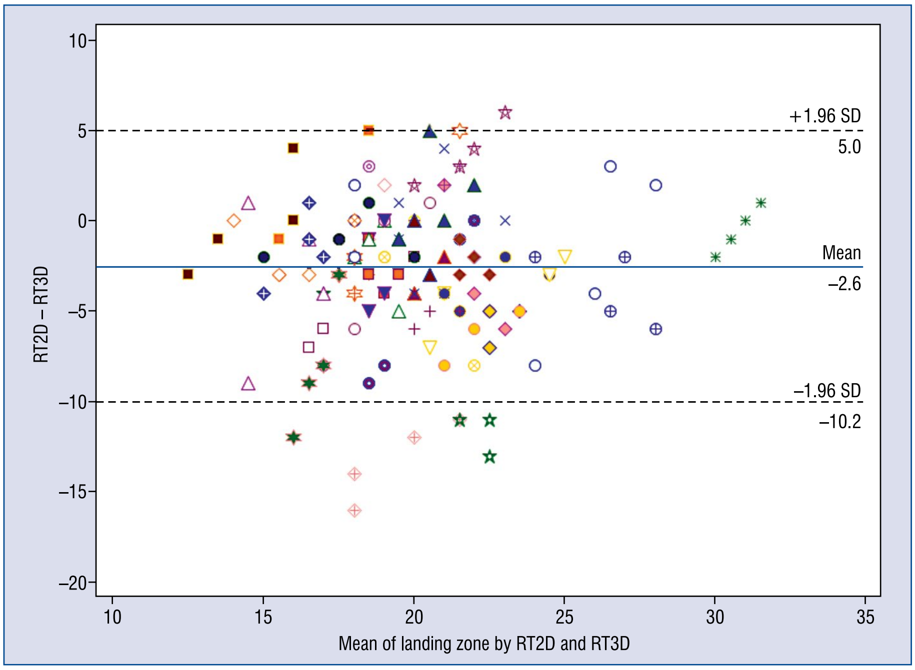

Figure 3. Bland-Altman plot with multiple measurements per subject for landing zone assessed with real-time two-dimensional transesophageal echocardiography (RT2D TEE) and real-time three-dimensional transesophageal echocardiography (RT3D TEE).

were found in repeated analysis of RT2D TEE images. No such differences were seen in the RT3D TEE measurements. The inter-observer variability for RT2D TEE and RT3D TEE data is presented in Table 2 (primary analysis and reanalysis).

The Bland-Altman plot with multiple measurements per subject including repeated measurements of the landing zone performed by both echocardiographers showed that the arithmetic mean difference between RT2D TEE and RT3D TEE dimension was 2.6 mm, and the lower and upper limits of difference were –10.2 mm and 5.0 mm, respectively (Fig. 3). Such differences may have an effect on the selection of occluders.

Intra-observer variability was performed for both echocardiographers. The analysis of ostium and landing zone measurements obtained with RT2D TEE differed significantly for both echo-

Table 3. Summary of intra-observer variability assessment for echocardiographer A and B (p value for T-test for dependent samples).

	P value	
	Echocardiographer A	Echocardiographer B
RT2D TEE Ostium	0.03	< 0.01
RT3D TEE Ostium	NS	NS
RT2D TEE Landing zone	0.03	0.01
RT3D TEE Landing zone	NS	NS

RT2D TEE — real-time two-dimensional transesophageal echocardiography; RT3D TEE — real-time three-dimensional transesophageal echocardiography; NS — not significant

cardiographers. No such differences were seen in RT3D TEE analysis (Table 3).

Based on the dimension of the landing zone obtained with RT2D TEE and the sizing charts provided by the manufacturer, the suggested device size was assigned for each subject. The same was performed for the data obtained with RT3D TEE. The inter-rater agreement (kappa) between the size of the implanted device and that selected with RT3D TEE was good (weighted kappa = 0.68), whereas that selected with RT2D TEE was only fair (weighted kappa = 0.28) (Table 4A, B).

Discussion

Appropriate occluder sizing is crucial for the safety and efficacy of LAAO. A TEE follow-up of patients randomized for LAAO with the Watchman device in the PROTECT-AF study revealed that up to 32% of implanted patients had at least some degree of peri-device flow at 1 month [15]. Although presence of peri-device leak was not associated with an increased risk of thromboembolism in that study, leaks over 5 mm in width indicate insufficient protection against ICS. Underestimation of the landing zone dimension increases the risk of peri-device leak and is a risk factor for early device embolization [16], whereas excessive oversizing may increase the risk of left LAA wall tear or compression of the adjacent structures.

Different imaging modalities, such as CCT, TEE, magnetic resonance imaging and fluoroscopy are used to determine LAA anatomy [17]. Although CCT and fluoroscopy have been shown to facilitate better assessment of LAA than TEE, the latter still remains the standard tool for guidance of LAAO procedures.

Clemente et al. [12] performed a pre-operative evaluation of LAA with TEE, CCT, intracardiac echocardiography, and CCA in 66 consecutive patients who underwent LAAO with the Amplatzer Cardiac Plug [12]. LAA diameters measured with CCT correlated with the diameters obtained with CCA and intracardiac echocardiography, but were slightly larger. TEE had a lower correlation with other imaging methods and a tendency to underestimate the LAA diameter. The authors concluded that CCT reduced device malposition because of under sizing. Similar findings were also reported by Vaitkus et al. [18] who found that CCT enables better visualization of LAA geometry and appropriate occluder selection. However, comparison between CCT and TEE for LAA evaluation was based on 2D imaging modality. Moreover, Budge et al. [19] compared the results of RT2D TEE with those obtained with planar CCT, and 3D segmented computed tomography reconstructions. They concluded that LAA orifice measurements were not interchangeable using these imaging modalities. The mean LAA orifice diameter in segmented CCT was larger (28.5 ± 4.5 mm) than planar CCT and TEE (26.3 ± 4.1 mm and 26.1 ± 6.4 mm, respectively).

The feasibility and accuracy of RT3D TEE in LAA morphology assessment was performed by Shah et al. [20]. The feasibility of RT3D TEE for LAA geometry was studied in the first 37 patients, whereas RT2D TEE and RT3D TEE quantification of the LAA were compared in the subsequent 29 patients. In 8 patients the data also correlated with CCT results. The LAA orifice area on CCT correlated well with RT3D TEE data (r = 0.98) but not with RT2D TEE data (r = 0.13). The Bland-Altman analysis demonstrated that, compared with RT3D TEE, RT2D TEE systematically underestimated the LAA orifice area.

Recently Yosefey et al. [21] showed that RT3D TEE (24.5 ± 4.7 mm) vs. CCT (24.6 ± 5, p = NS) was more accurate in measuring the maximal LAA diameter compared to RT2D TEE (23.5 ± 3.9 mm)

Table 4A. Inter-rater agreement (kappa) for devices selected with real time two-dimensional transesophageal echocardiography (RT2D TEE) and the implanted devices. Weighted kappa 0.28.

Implanted device	Device by RT2D TEE											
	16	18	20	22	24	25	26	28	30	31	34	
16	0	0	0	0	0	0	0	0	0	0	0	0 (0.0%)
18	1	1	0	1	0	0	0	0	0	0	0	3 (7.5%)
20	0	0	1	0	0	1	0	0	0	0	0	2 (5.0%)
22	1	0	6	1	0	0	0	3	0	1	0	12 (30.0%)
24	0	1	0	0	0	1	0	2	0	0	0	4 (10.0%)
25	0	0	0	1	0	2	0	1	0	0	0	4 (10.0%)
26	0	0	0	1	0	1	0	2	0	1	0	5 (12.5%)
28	0	0	0	2	0	2	0	2	0	0	0	6 (15.0%)
30	0	0	0	0	0	0	0	0	0	1	0	1 (2.5%)
31	0	0	1	0	0	0	0	0	0	0	0	1 (2.5%)
34	0	0	0	0	0	1	0	0	0	1	0	2 (5.0%)
	2 (5.0%)	2 (5.0%)	8 (20.0%)	6 (15.0%)	0 (0.0%)	8 (20.0%)	0 (0.0%)	10 (25.0%)	0 (0.0%)	4 (10.0%)	0 (0.0%)	40

Table 4B. Inter-rater agreement (kappa) for devices selected with real time three-dimensional transesophageal echocardiography (RT3D TEE) and the implanted devices. Wighted kappa 0.62.

Implanted device	Device by RT3D TEE										
	18	20	22	24	25	26	28	30	31	34	
18	1	1	1	0	0	0	0	0	0	0	3 (7.5%)
20	0	1	1	0	0	0	0	0	0	0	2 (5.0%)
22	0	2	6	0	3	0	1	0	0	0	12 (30.0%)
24	0	0	0	3	0	0	0	1	0	0	4 (10.0%)
25	0	0	0	0	2	0	0	0	2	0	4 (10.0%)
26	0	0	0	0	1	2	2	0	0	0	5 (12.5%)
28	0	0	1	0	1	0	3	0	0	1	6 (15.0%)
30	0	0	0	0	0	0	1	0	0	0	1 (2.5%)
31	0	0	0	0	0	0	0	0	1	0	1 (2.5%)
34	0	0	0	0	0	0	0	0	1	1	2 (5.0%)
	1 (2.5%)	4 (10.0%)	9 (22.5%)	3 (7.5%)	7 (17.5%)	2 (5.0%)	7 (17.5%)	1 (2.5%)	4 (10.0%)	2 (5.0%)	40

vs. CTA ($p < 0.01$). However, the measurements were performed for the orifice, not the landing zone, which is the reference for occluder sizing. Moreover Nucifora et al. [22] showed higher correlation of CCT with RT3D TEE for assessment of the LAA orifice area compared to RT2D TEE ($r = 0.92$, 95% CI 0.85–0.95 and $r = 0.72$, 95% CI 0.55–0.83, respectively).

In accordance with the cited literature, results of the present study confirmed that the diameter of LAA ostium and LAA landing zone are considerably larger when assessed with RT3D TEE as compared with RT2D TEE. However, previous studies lacked a comparison between the results obtained with CCT or RT3D TEE and the actual fit of occluders used for LAAO. Neither the comparison of images after implantation nor the frequency of peri-device leak was analyzed for RT3D TEE or CCT. Despite previous recommendations for the use of RT2D TEE in occluder selection for LAAO, according to available research, the presented analysis shows the superiority of RT3D TEE over RT2D TEE for the first time. Moreover, RT3D TEE enables better imaging of the structures surrounding the LAA, thus reducing the probability of malposition. Use of RT3D TEE instead of RT2D TEE also generates practical advantages, such as avoiding potential complications, reducing radiation exposure, and/or shortening procedural times [23]. A possible limitation of RT3D TEE may be the lack of standards for obtaining RT3D TEE images. Nevertheless, it is becoming an elementary navigation method for percutaneous procedures e.g. percutaneous mitral valve repair [24].

Although the accuracy of LAA assessment is similar for both RT3D TEE and CCT, the first does not require contrast agents. It is especially important in patients with renal failure qualified for LAAO. Other advantages include cost effectiveness, lack of radiation, and lesser time consumption.

Conclusions

There are significant differences between RT2D TEE and RT3D TEE in the assessment of the LAA ostium and landing zone diameters. The results showed significantly larger dimensions of both the ostium and the landing zone obtained with RT3D TEE. RT2D TEE measurement of the ostium and landing zone dimensions were associated with significant inter- and intra-observer variability; no such differences were found for RT3D TEE results. RT3D TEE has a better agreement with the implanted occluders than RT2D TEE.

Conflict of interest: W. Streb, K. Mitręga and Z. Kalarus are proctors of St. Jude Medical.

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