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Percutaneous Interventions for Left Atrial Appendage Exclusion

Options, Assessment, and Imaging Using 2D and 3D Echocardiography

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CME Objective for This Article: To learn about the currently available left atrial appendage (LAA) exclusion devices, and how to use 2D and 3D TEE to evaluate the LAA anatomy, its suitability for device placement, how to use echo to size devices, guide device placement and evaluate the results of LAA device closure.

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ABSTRACT

Percutaneous left atrial appendage (LAA) exclusion is an evolving treatment to prevent embolic events in patients with nonvalvular atrial fibrillation. In the past few years multiple percutaneous devices have been developed to exclude the LAA from the body of the left atrium and thus from the systemic circulation. Two- and 3-dimensional transesophageal echocardiography (TEE) is used to assess the LAA anatomy and its suitability for percutaneous closure to select the type and size of the closure device and to guide the device implantation procedure in conjunction with fluoroscopy. In addition, 2- and 3-dimensional TEE is also used to assess the effectiveness of device implantation acutely and on subsequent follow-up examination. Knowledge of the implantation options that are currently available along with their specific characteristics is essential for choosing the appropriate device for a given patient with a specific LAA anatomy. We present the currently available LAA exclusion devices and the echocardiographic imaging approaches for evaluation of the LAA before, during, and after LAA occlusion. (J Am Coll Cardiol Img 2015;8:472–88) © 2015 by the American College of Cardiology Foundation.

The left atrial appendage (LAA) is a tubular, blind-ended pouch attached to the main body of the left atrium (LA). It is the source of cerebral thromboembolism in approximately 90% of patients with nonvalvular atrial fibrillation (AF) (1,2).

LAA occlusion or exclusion to prevent embolism in patients with nonvalvular AF by implanting a percutaneously delivered device to exclude the LAA cavity from the systemic circulation has evolved since the first implantation of an LAA occlusion device in 2001 (3). Currently there are 3 devices (**Figure 1**) available for percutaneous implantation within the LAA and one suture-based technology to occlude the LAA (**Figure 2**). European guidelines for management of AF now recommend that percutaneous LAA closure may be considered in high stroke risk patients with contraindications for long-term oral anticoagulation (class IIb indication, level of evidence B) (4).

Transesophageal echocardiography (TEE) is the main imaging modality used to assess LAA anatomy, aid in the selection of a suitable device and size, and identify anatomic contraindications. Two-dimensional (2D) and 3-dimensional (3D) TEE are used in conjunction with fluoroscopy to guide the procedure, evaluate results after device placement, and monitor for complications. In this review, we focus on current echocardiographic imaging approaches for the evaluation of the LAA before, during, and after LAA occlusion, and on the different imaging aspects in regard to the currently available devices.

CURRENT DEVICES FOR PERCUTANEOUS LAA OCCLUSION OR EXCLUSION

As shown in the **Central Illustration**, as well as in **Figures 1 and 2**, knowledge of the different devices and their characteristics is important for optimal patient selection and successful guidance of an LAA closure procedure. All LAA closure devices described in this review are available for clinical use in Europe. In the United States, the endoluminally implanted devices can only be used as part of a clinical trial. The LAA occluder device (Watchman device, Boston Scientific, Natick, Massachusetts) received FDA approval very recently in March 2015. The LAA ligation device (LARIAT suture device, SentreHEART, Inc., Redwood City, California) is approved by the Food and Drug Administration for suture placement and knot tying in surgical applications; however, it is not approved specifically for treatment of stroke prevention in patients with AF.

ENDOLUMINAL LAA CLOSURE DEVICES. LAA occluder device. The LAA occluder device (**Figure 1A**) is a self-expanding system with a nitinol frame covered with a permeable 160 μm polyethylene terephthalate fabric on the LA side of the device. Ten active fixation hooks are placed around the circumference. There are

ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation

CMR = cardiac magnetic resonance

LA = left atrium

LAA = left atrial appendage

MDCT = multidetector computed tomography

RT = real time

TEE = transesophageal echocardiography

TTE = transthoracic echocardiography

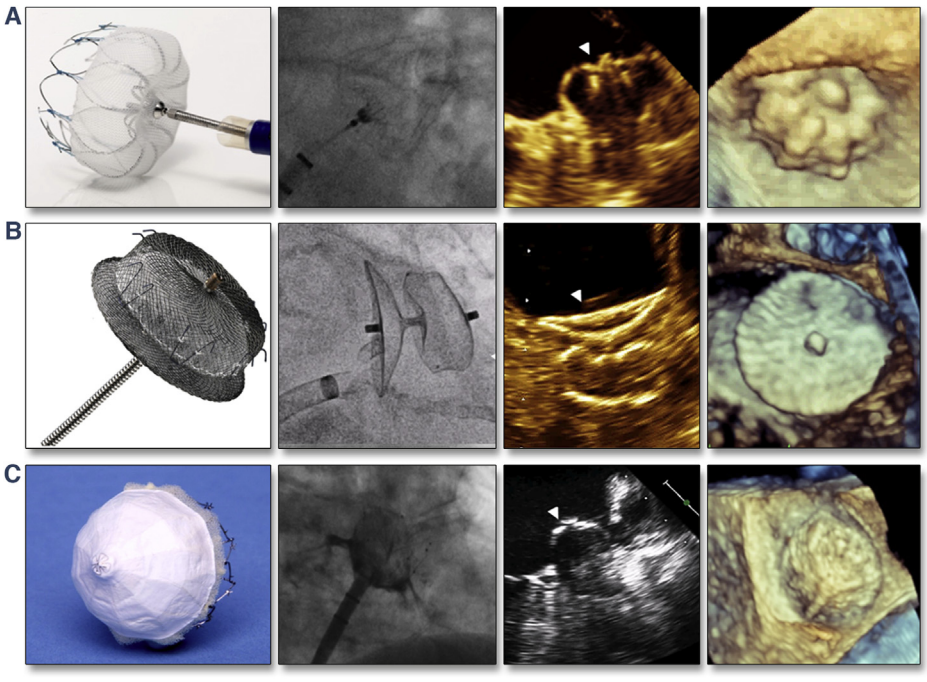
TS = transseptal

more data on outcomes available on the LAA occluder device than on any other LAA occlusion system. Randomized studies with the LAA occluder device (PROTECT-AF [WATCHMAN Left Atrial Appendage System for Embolic PROTECTion in Patients With Atrial Fibrillation] trial; n = 707; 463 device/244 control) confirmed noninferiority for LAA occlusion compared with oral warfarin therapy with regard to the primary composite endpoint of stroke, cardiovascular or unexplained death, and all-cause death (5–7). After 3.8 years of follow-up among PROTECT-AF patients, percutaneous LAA closure met criteria for both noninferiority and superiority, compared with warfarin, for preventing the combined outcome of stroke, systemic embolism, and cardiovascular death, as well as superiority for cardiovascular and all-cause mortality (8).

In the randomized PREVAIL (Evaluation of the Watchman LAA Closure Device in Patients With Atrial Fibrillation Versus Long Term Warfarin Therapy) trial (n = 407; 269 device/138 control), a continuum of the PROTECT-AF trial, LAA occlusion was noninferior to warfarin for ischemic stroke prevention or systemic embolism >7 days post-procedure. Although noninferiority was not achieved for overall efficacy, event rates were low and numerically comparable in both treatment arms (device implantation vs. chronic warfarin therapy) (9). Registry data on 610 patients have also been published (10–12).

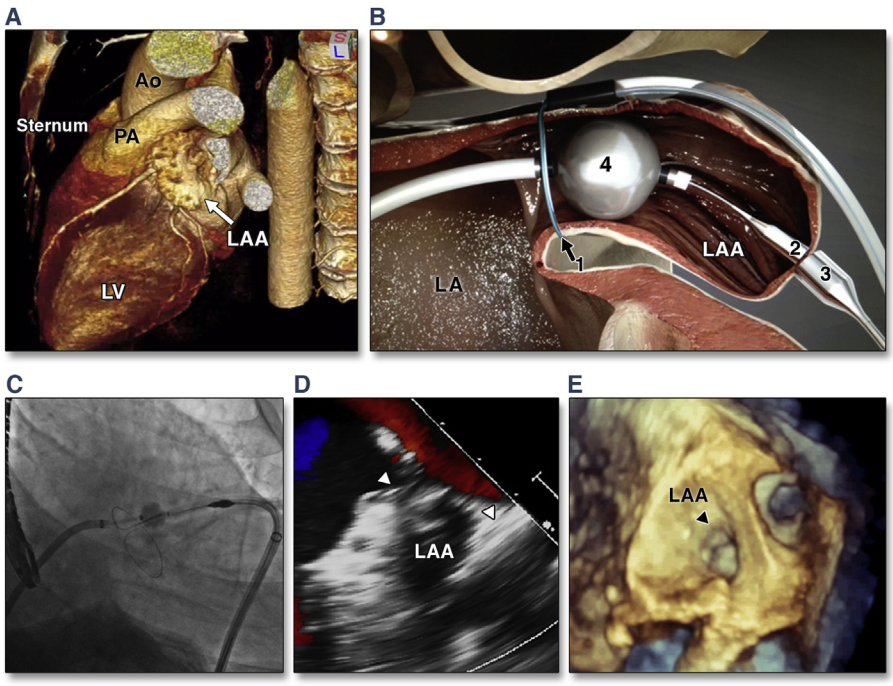
First Generation LAA Plug. The first generation LAA plug (Amplatzer Cardiac Plug, St. Jude Medical, Inc., St. Paul, Minnesota) (**Figure 1B**) device is designed to occlude the full cross-sectional area of the LAA orifice. The device is made of a flexible braided nitinol mesh and has 2 major components: a distal lobe with 6 pairs of hooks attached and a proximal disc to cover the ostium. A central waist constitutes an articulating, compliant connection between the disc and the lobe. Nonrandomized trials with the first generation LAA plug demonstrate feasibility, effectiveness in reducing thromboembolic cerebral events, and a high

FIGURE 1 Endoluminal LAA Occlusion Devices



Different endoluminal LAA occlusion devices **(far left column)**. **(A)** LAA occluder device. **(B)** First generation LAA plug. **(C)** Flexible LAA occlusion device (device images with permission from Boston Scientific, St. Jude Medical, Inc., and Coherex Medical, Inc.). The appearance of the different devices using different imaging modalities after device placement is shown (fluoroscopy **[left column]** followed by echocardiography 2D TEE **[middle column]** and 3D TEE **[right column]**). 2D = 2-dimensional; 3D = 3-dimensional; LAA = left atrial appendage; TEE = transesophageal echocardiography.

FIGURE 2 LAA Ligation Device and Different Imaging Modalities Pre- and Post-Procedure



(A) Computed tomography imaging of favorable LAA anatomy is shown in a lateral view with the LAA in the foreground. The LAA is lateral to the PA (with permission from SentreHEART, Inc.). The major component of the system consists of a collapsible snare with a pre-tied suture loop **(1)**. **(B)** Via transseptal access, a magnetic wire is placed inside the LAA **(2)**. A second magnetic wire is introduced via a percutaneous epicardial approach and directed toward the magnetic wire in the LAA **(3)**. Once both magnets are engaged, a magnetic wire bridge is created **(2, 3)**. Using this endocardial/epicardial magnetic wire bridge as guide rail an endocardial compliant balloon is delivered, which is inflated at the LAA ostium to mark the "landing zone" for the suture **(4)**. Coming from the epicardial side the LAA ligation device suture-loop is inserted over the wire, placed around the LAA, and snared close to the LAA ostium above the inflated balloon **(1)**. The suture is tightened by using a pre-tied one-way slip knot, ultimately resulting in LAA closure. **(C)** Fluoroscopic image of the suture-loop placed around the LAA above the inflated balloon. **(D)** A 2D TEE image with color Doppler demonstrating no residual flow within the LAA cavity. The **white arrowhead** points at the location of the suture close to the LAA ostium. **(E)** A 3D TEE enface image of the LAA ostium after successful LAA closure with the LAA ligation device. The **black arrowhead** points at the LAA ostium. Ao = aorta; LA = left atrium; LV = left ventricle; PA = pulmonary artery; other abbreviations as in Figure 1.

rate of technical success (13-16). Data on nearly 2,000 first generation LAA plug patients are published. Most of them were implanted in Europe, 20 in Asia, and 52 in Canada (10,13-17). A second-generation LAA plug (AMPLATZER Amulet LAA occluder, St. Jude Medical, St. Paul, Minnesota) is also being tested in clinical trials (18). The second generation LAA plug allows for larger LAAs to be treated. This device design has a slightly larger disc than the first generation LAA plug to better occlude the LAA ostium. The waist and the lobe are longer compared with the first generation LAA plug and the number of stabilizing wires surrounding the device body is increased for improved device flexibility and stability.

Flexible LAA occlusion device. The flexible LAA occlusion device (Coherex WaveCrest, Coherex Medical, Inc., Salt Lake City, Utah) (Figure 1C) was approved for use in Europe in September 2013. This umbrella-shaped device consists of a nitinol frame with 20 anchoring points. An occlusive, nonthrombogenic expanded polytetrafluoroethylene membrane covers the LA side of the device. A polymer foam around the device faces the LAA side. Preliminary clinical experience with the flexible LAA occlusion device (n = 63) demonstrated high closure rates of 97% and a good safety profile (19).

EPICARDIAL APPROACH FOR LAA LIGATION. Figure 2 shows the LAA ligation device. This device is designed to occlude the LAA percutaneously using a suture. The percutaneous catheter-based LAA ligation using the LAA ligation device has been shown to

be feasible and effective in humans and complete closure of the LAA has been achieved in observational studies and 1 retrospective multicenter study in the United States (n = 277 with successful device implantation) (20-23).

IMAGING MODALITIES AND GENERAL IMAGING ASPECTS IN PROCEDURE PLANNING

As described in **Table 1** and shown in **Figure 3**, it is useful to divide the LAA anatomically into 3 regions: 1) the ostium; 2) the neck; and 3) the lobar region. There is broad variability in LAA morphology, a fact that complicates adequate evaluation (24). LAA ostium diameters range from 10 to 40 mm, its length from 16 to 51 mm, with volumes from 0.7 to 19.2 ml. On postmortem evaluation it was demonstrated that LAA from patients with AF have 3 times the volume of those who were in sinus rhythm (25). Patients with chronic AF frequently have LAA remodeling in which there is dilation, stretching, and reduction in pectinate muscle volume, as well as endocardial fibroelastosis (25).

Important aspects for LAA occlusion include the correct sizing of the landing zone diameters for the selected device and the measurement of the depth and orientation of the main anchoring lobe and the number and origin of additional lobes. In >50% of patients, 2 or more lobes are present (26,27).

Because of the substantial variations in LAA anatomy that impact device selection and efficacy, as detailed in **Table 1**, an accurate assessment of anatomic LAA characteristics is crucial before an LAA closure procedure. LAA imaging modalities used include transthoracic echocardiography (TTE), TEE, multidetector computed tomography (MDCT), and cardiac magnetic resonance (CMR).

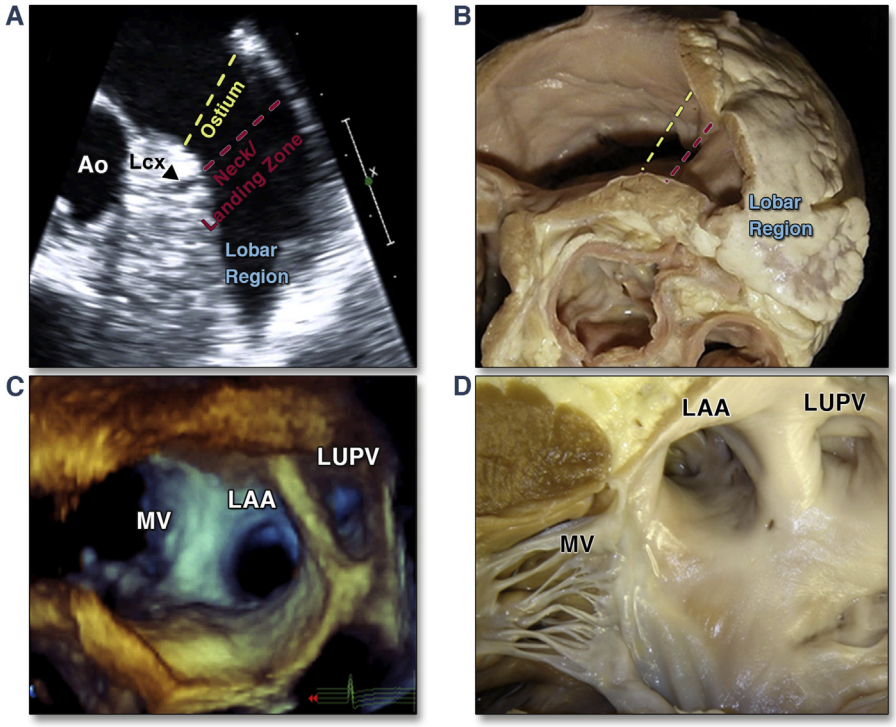
TTE. Before an LAA closure procedure, 2D and 3D TTE is used to evaluate LA dimensions and volumes (28,29) and left ventricular function (a risk factor for thromboembolism [30]), and to exclude contraindications for LAA closure (e.g., patients with valvular AF) or significant valve disease requiring surgery or patients with a left ventricular thrombus or a mechanical heart valve who require chronic anticoagulation.

TABLE 1 LAA Regions, Their Anatomic Characteristics, Neighboring Structures, and Specific Considerations With Regard to Percutaneous LAA Closure

LAA Region	Anatomic Description	Anatomic Characteristics	Neighboring Structures	Specific Considerations With Regard to LAA Closure
The ostium	Opening from the LA to the LAA (the ostium is usually a well-defined plane)	Generally oval in shape (26,27) The wall around the ostium can be very thin (27)	MV (27) Left upper pulmonary vein (27)	A very eccentric LAA ostium may be problematic for device placement (risk of peridevice leakage) Thin wall areas increase the risk of perforation The MV or the left upper pulmonary vein may be altered by a device
The neck	The ostium opens to a neck region that constitutes a tubular junction between the ostium and the lobar region	Pits or troughs and areas of thin atrial wall were found in ~58% of hearts within a ~21-mm radius from the ostium (27) Secondary lobes may originate close to the ostium	Circumflex coronary artery (27) Left anterior descending artery (27) Sinus node artery (in ~30%) (27)	A severe angulation between the ostium and the neck may cause technical problems Areas of thin wall increase the risk of perforation A lobe that originates very close to the ostium may stay unsealed Coronary arteries can be at risk during LAA occlusion
The lobar region	Largest and most variable distal part of the LAA	1-5 lobes may be present (26,27) Small crevices and areas of very thin wall were found (27)	The tip of the appendage overlaps the base of the pulmonary trunk, the left coronary artery, or its anterior branch and the great cardiac vein at varying levels (27) The left phrenic nerve runs along the pericardium overlaying the LAA (27)	The main anchoring lobe needs to be long enough to accommodate the selected device An LAA, which is located underneath a pulmonary artery, is not suitable for a suture approach Pericardial access may potentially cause damage to the left phrenic nerve Areas of thin wall increase the risk of perforation Coronary arteries can be at risk during LAA occlusion Specific morphologies (e.g., a chicken wing morphology) may need specific implantation strategies for LAA closure

LA = left atrium; LAA = left atrial appendage; MV = mitral valve.

FIGURE 3 Echo-Anatomy of the LAA



The LAA regions are illustrated in a 2D TEE view (45°) **(A)** and in a corresponding anatomic image **(B)**. The **black arrowhead** in **(A)** marks the Lcx. Relationship between the LAA, the LUPV, and the MV are shown in a 3D TEE aspect **(C)** and in an anatomic picture **(D)**. Lcx = left circumflex coronary artery; LUPV = left upper pulmonary vein; MV = mitral valve; other abbreviations as in Figure 1.

TEE. Pre-procedure TEE is the main imaging modality because the LAA cannot be definitively assessed by TTE. The close relationship of the esophagus and the LA allows detailed imaging of the LAA in most patients (31). Among other things TEE is used to exclude thrombi in the LA and LAA (32). 3D TEE is helpful in differentiating a thrombus from LAA pectinate muscles (33). In case there is uncertainty about the presence of a clot, the use of ultrasound contrast is helpful to identify these thrombi (34). Pre-procedure TEE is also used to exclude other sources of embolism, such as cardiac masses and thrombi (3D TEE has shown to be more accurate compared with 2D TEE in characterizing diameters, types, surface features, mobility, and sites of intracardiac masses, and spatial relationship to surrounding structures [35-38]) as well as aortic arch atheroma. If an LA/LAA thrombus is diagnosed, anticoagulant therapy should be given until the thrombus has resolved by TEE before proceeding to implantation of an LAA occlusion device.

A careful multiplane 2D TEE analysis (0° to 180°) (39) improves the understanding of complex LAA morphologies. Slight rotations of the probe are useful to assess all lobes adequately and to depict additional lobes. 3D TEE provides a more detailed assessment and quantitative analysis of the LAA orifice area compared with 2D TEE (40,41).

MDCT AND CMR. Although TEE is the most widely used imaging modality for LAA evaluation, MDCT and CMR are emerging imaging techniques for the pre- and post-procedural assessment of thrombus formation, LAA anatomy and function, device assessment, and the detection of complications post-procedure, which can provide complementary or additional information regarding the LAA.

MDCT. MDCT acquires 3D volumetric data sets of the entire heart, which can be reconstructed by using numerous planes at different points in time during the cardiac cycle thus providing accurate assessment of LAA anatomy. MDCT accurately depicts the morphology of the LAA ostium, the perimeter of the LAA orifice, and the angle of the first LAA bend. Measurement of the LAA ostial perimeter is the most

reproducible parameter for sizing an LAA occluder rather than the measurement of its maximum diameter (42,43). MDCT has a 100% sensitivity for excluding LAA thrombi (44). However, it has a high rate of false positive tests and poor interobserver variability (45).

Different LAA morphologies were described recently by the use of MDCT to categorize the various LAA shapes: windsock, cactus, cauliflower, and chicken wing (46,47), but the impact of these different morphologies on procedural outcome after LAA closure is unknown. Limitations of MDCT include ionizing radiation, a lower temporal resolution than TEE, and it cannot be performed during device deployment.

CMR. Although experience is limited, CMR is an alternative noninvasive imaging modality in pre- and post-procedural LAA assessment to accurately visualize LAA size and function, and to detect thrombi in patients with AF with effectiveness comparable with TEE (48–52). LAA devices are typically made from metals that include nitinol, titanium, titanium alloy, MP35N, 316L stainless steel, and 304V stainless steel. At 1.5-T, only devices made from 304V stainless steel displayed weakly ferromagnetic qualities. The LAA occluder device has been tested and findings indicate that this device can be safely used at 3.0-T (53). In post-procedural evaluation contrast-enhanced CMR is feasible to confirm occluder placement and to detect residual peridevice leaks (54).

Advantages of CMR include no radiation exposure or need for iodinated contrast. However, limitations include the lower spatial resolution, prolonged examination times, the dependence on the ability to perform adequate breath holds, and limited ability to use CMR in patients with implanted pacemakers or defibrillators or during the device implantation procedure.

SPECIFIC IMAGING ASPECTS IN PRE-PROCEDURE PLANNING

DEVICE SIZING FOR ENDOLUMINAL OCCLUSION DEVICES. Device sizing is of paramount importance to ensure a stable device position and optimal sealing of the LAA. Undersizing of the device has the potential risk of device migration or embolization and may favor peridevice leakage. Oversizing of the device should also be avoided because this may cause cardiac perforation, pericardial effusion, and cardiac tamponade (11,55,56).

To avoid undersizing, the measurements for device selection should be performed when the LAA size is largest, namely at the end of ventricular systole and under normal LA filling conditions. To accurately define ostium diameters, landing zone diameters and LAA depth measurements should be obtained preprocedurally in different echocardiographic views and intraprocedurally also with the addition of fluoroscopy.

As shown in **Figure 4**, when 2D TEE is used (left panel), the required measurements are obtained by rotating the TEE transducer array through at least 4 different mid-esophageal planes (typically at ~0°, ~45°, ~90°, and ~135°). Because the LAA orifice is most commonly oval in shape (26) larger orifice diameters can often be found on 120° to 135° planes rather than at 45° or 90° (57).

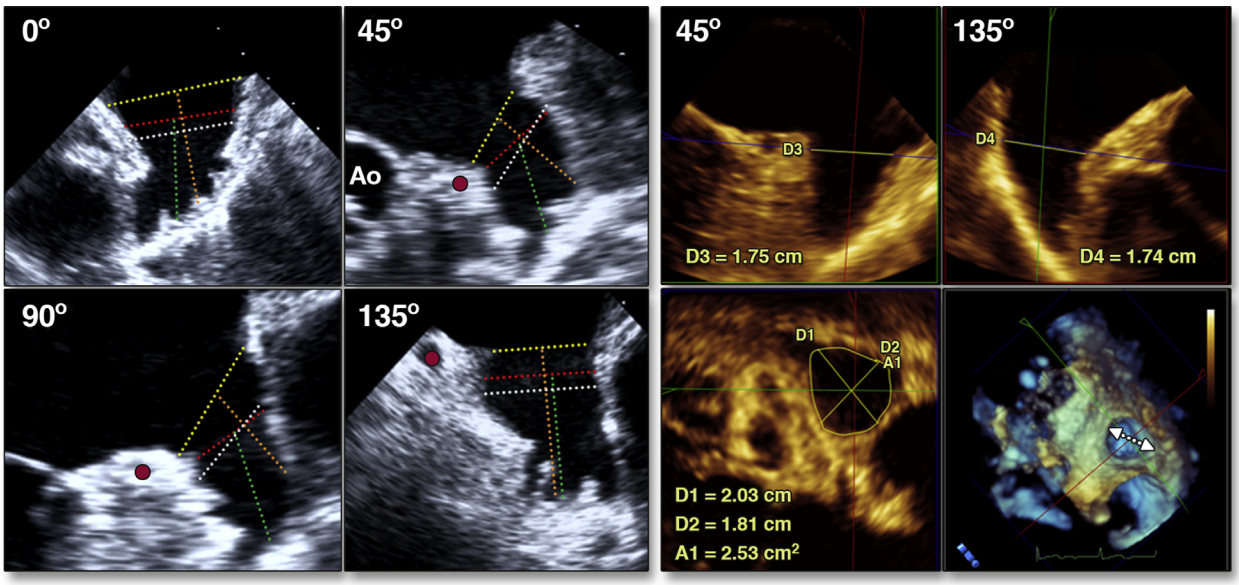
Figure 4 (right panel) provides an additional example of real-time (RT) 3D TEE of the LAA. Several studies validate that RT 3D TEE more accurately assesses the true LAA orifice size. RT 3D TEE was found to be closely related to CT measurements (40,41), whereas 2D TEE tends to underestimate the LAA orifice area (40,41,58,59).

The choice of an appropriate occlusion device depends on accurate measurements of the landing zone diameters. To achieve a secure and stable device position, the size of the occlusion device is usually selected to be a few millimeters larger in diameter than the measurements of the landing zone (**Table 2**). The maximum length of the anchoring lobe has to be measured in addition (in the expected axis of the device) to ensure that this lobe has enough space to accommodate the selected device. As illustrated in **Figure 4** and **Table 2**, different device designs require different measurements because the different endoluminal occluder systems vary slightly.

The angle between the ostium, the neck, and the main anchoring lobe should be evaluated because it can influence the choice of the puncture site and/or the curve of the delivery sheath. The number and origin of additional LAA lobes also needs to be assessed.

SPECIFIC LAA MORPHOLOGIES. Because some LAA morphologies are more challenging for device closure than others, LAA anatomy should be adequately defined before any planned procedure. A secondary lobe originating close to the ostium can pose problems, because it may not be covered after device deployment. Two large lobes of a similar size separated by a large rim in between them may cause problems if the remaining proximal portion of the LAA is too short to accommodate a device.

FIGURE 4 2D and 3D TEE: Measurements of LAA Dimensions



On the left side 2D TEE measurements of the landing zone diameters and the maximum length of the LAA in the axis of the device are demonstrated in 4 different 2D imaging planes. LAA occluder device: the landing zone measurement **(dotted red line)** is performed from the inferior part of the LAA ostium at the level of the circumflex coronary **(red dot)** to a point 1–2 cm distally to the tip of the rim to the LUPV. The LAA depth **(dotted green line)** is measured perpendicular to that measurement. LAA plug devices: the measurement of the landing zone diameter in the anchoring lobe is obtained ~10 mm distally from the ostial plane **(dotted yellow line)** into the lobe **(dotted white line)**. The depth of the main lobe **(dotted orange line)** is measured in the expected axis of the device. Flexible LAA occlusion device: the landing zone measurement for the flexible LAA occlusion device is performed in a similar way as for the LAA occluder device **(dotted red line)**. The measurement of the depth plays a minor role as the level of the landing zone marks the distal occluder margin (unlike other devices). The image on the right side gives an example of the 3D TEE measurement of the landing zone. In this post-processing analysis 45° **(upper left panel)** and 135° **(upper right panel)** views are shown. The **yellow line** demarcates the landing zone measurement. An enface plane at the level of the landing zone is shown on the **lower panel on the left side**. Diameters **(D1 and D2)** and the area **(A1)** are measured. An additional 3D enface view **(right side, lower panel)** shows the LAA orifice in relation to neighboring structures. The **white double arrowhead** marks the largest diameter that would be missed by measuring only along the **red** or **green cropping line**. Abbreviations as in Figures 1 and 3.

A cone-shaped LAA is characterized by progressive reduction in dimensions from its orifice to its distal tip. A major concern with this morphology is that compressive forces transmitted by the distal LAA wall onto the closure device are more pronounced than in the proximal LAA, which can result in compressive forces that would push the device out of the LAA toward the orifice and into the LA. The risk of device migration or embolization is therefore increased in these patients. Moreover, this may be further aggravated by the lack of trabeculations in the LAA landing zone region. When an LAA plug device is used, it has to be taken into consideration that the ostium diameter is considerably larger than the landing zone diameter in such morphologies. Consequently, the disc may be too small to seal the ostium adequately in some patients. Finding a suitable LAA plug size can be challenging in these patients.

A chicken wing LAA morphology, characterized by an early (<20 mm from the ostium) and severe bend, is one of the most difficult anatomic variations for LAA closure. Specific implantation techniques may be necessary to achieve LAA occlusion in these cases (60). We have found that the chicken wing morphology is generally best evaluated using the long axis TEE planes (120° to 135°).

LAA ASSESSMENT FOR EPICARDIAL LAA LIGATION. When LAA closure with the LAA ligation device is planned a spiral CT has to be obtained to clarify LAA orifice diameters and sizes and LAA orientation and location. Patients with an LAA width >40 mm or in whom the LAA is located under a pulmonary artery (20) are not suitable for suture placement. In patients with 2 large lobes that are pointing in different directions, the placement of the suture loop can be difficult. Patients with prior cardiac surgery or pericarditis also are not suitable for the LAA ligation

TABLE 2 Morphologic Device-Specific Requirements

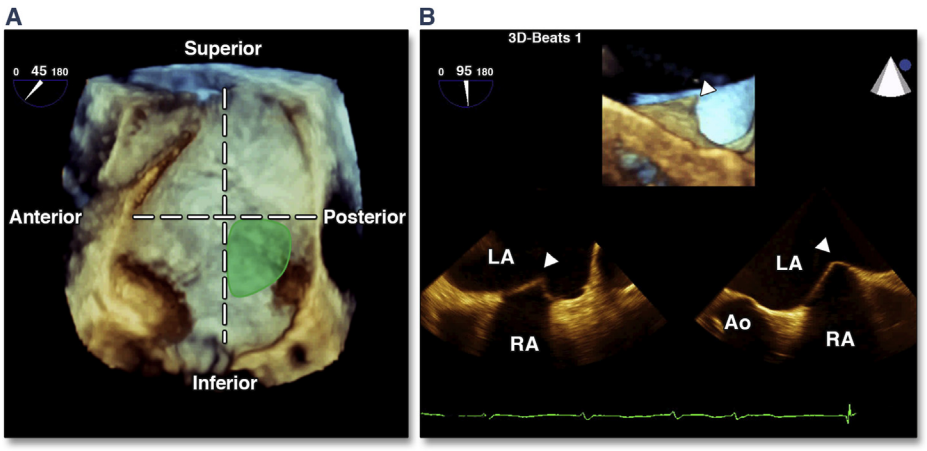
	Endoluminal			Extraluminal
	LAA Occluder Device	First Generation LAA Plug/ Second Generation LAA Plug	Flexible LAA Occlusion Device	LAA Ligation Device
Available device sizes	5 device sizes: 21, 24, 27, 30, 33 mm	First generation LAA plug: 8 device sizes: 16, 18, 20, 22, 24, 26, 28, 30 mm (the disc is 4 mm larger for device sizes up to 22, and 6 mm larger for device sizes 24–30 mm) Second generation LAA plug: 8 device sizes: 16, 18, 20, 22 (lobe length 7.5 mm, waist length 5.5 mm; disc size = lobe size + 6 mm); 25, 28, 31, 34 mm (lobe length 10 mm, waist length 8 mm; disc size = lobe size + 7 mm)	3 device sizes: 22, 27, 32 mm	Only 1 device size: a 40-mm pre-tied suture loop
Ostium diameter*	–	The ostium diameter has to be smaller than the disc size of the selected device	–	<40 mm (CT required)
Definition of where to measure the landing zone diameters for endoluminal devices* (by TEE)	Measured from the inferior part of the LAA ostium at the level of the circumflex coronary artery to a point 1–2 cm distally to the tip of the rim to the LUPV	Measured at ~10 mm distally from the ostial plane into the lobe	Measured from the inferior part of the LAA ostium at the level of the circumflex coronary artery to a point 1–2 cm distally to the tip of the rim to the LUPV	–
Required landing zone diameters	17–31 mm	First generation LAA plug: 12.6–28.5 mm Second generation LAA plug: 11–31 mm	15–29 mm	Ostium diameter <40 mm (CT required) Sizes up to 70 mm in length and 20 mm in height can be treated
Choice of device size	2–4 mm larger than the largest measured diameter	1.5–3.4 mm larger than the largest measured diameter	3–8 mm larger than the largest measured diameter	–
Required depth of main anchoring lobe (in the axis of the device)*	≥19 mm for the smallest device size (21 mm) The length of the device progressively increases as device diameter increases	≥10 mm for the first generation LAA Plug and second generation LAA plugs up to 22 mm. For larger second generation LAA plugs: >12mm	≤10 mm	–
General morphological exclusion criteria	Presence of a thrombus/cardiac tumor Comorbidities other than atrial fibrillation that require chronic anticoagulation therapy Rheumatic valvular disease Active endocarditis			
Additional morphological exclusion criteria	LVEF <30%; pericardial effusion >2 mm; high risk PFO; history of ASD repair or present ASD/PFO device; significant mitral valve stenosis; complex atheroma with mobile plaque of the descending aorta (5)	Presence of an ASD/PFO device; history of surgical ASD/PFO repair; history of stroke and unrepaired PFO; moderate to severe aortic or mitral valve stenosis or regurgitation; pericardial effusion; complex atheroma with mobile plaque of the descending aorta and/or aortic arch (first generation LAA plug registry-long-term follow-up protocol)	LVEF <30%; mitral valve stenosis <1.5 cm^2; pericardial effusion >5 mm pre-procedure; presence of a PFO that demonstrates a large shunt and/or atrial septal aneurysm with >10 mm excursion; (flexible LAA occlusion device I exclusion criteria; ongoing trial)	LVEF <30%; a superiorly orientated LAA with the LAA apex directed behind the pulmonary trunk; bilobed or multilobed LAA in which lobes are orientated in different planes exceeding 40 mm; a posteriorly rotated heart; pericardial adhesions (patients with prior cardiac surgery/pericarditis/history or radiation therapy were also excluded because of the high likelihood of pericardial adhesions) (20)

*All measurements should be performed at the ventricular end-systole and under normal left atrial filling pressures.

ASD = atrial septal defect; CT = computed tomography; LUPV = left upper pulmonary vein; LVEF = left ventricular ejection fraction; PFO = patent foramen ovale; TEE = transesophageal echocardiography; other abbreviations as in Table 1.

device procedure because of the high likelihood of residual pericardial adhesions, which would interfere with placement of the LAA ligation device. A TEE pre-LAA ligation device procedure is important to exclude LAA thrombi, and it provides detailed information on the number and orientation of lobes. However, it is not as important for device guidance as TEE is with the implantable LAA occlusion devices (61).

FIGURE 5 TS Puncture

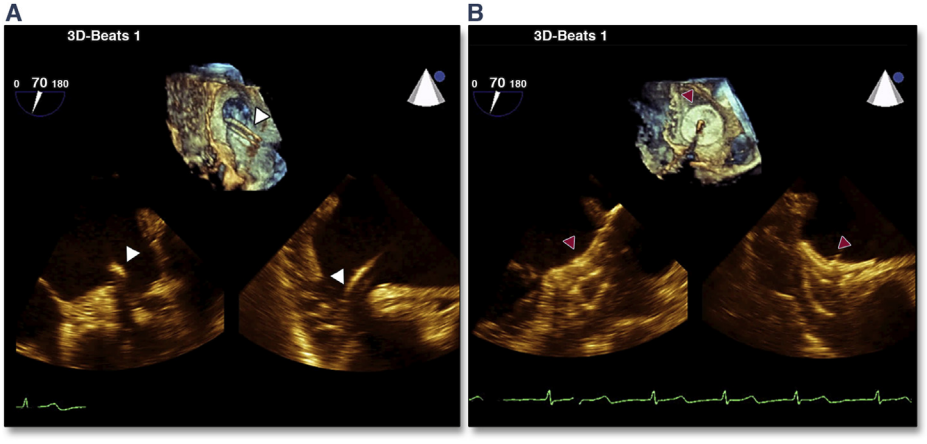


(A) Viewed from a position in the middle of the interatrial septum **(crossing of the white dashed lines)** the preferred TS puncture site is located usually slightly posterior and inferior as demonstrated in **A (green area)** in a left atrial 3D TEE aspect. **(B)** Simultaneous 3D TEE **(top)** and X-plane imaging **(bottom)** demonstrates the tent-like indentation of the interatrial septum **(white arrowheads)**. This imaging approach facilitates the determination of the preferred puncture site (Online Video 1). Factors that can impact the TS puncture, such as the size and location of the fossa ovalis, the thickness of the interatrial septum, the presence of a persistent foramen ovale, an atrial septum defect, an atrial septum aneurysm, or an eustachian valve, should be assessed in addition (not shown). RA = right atrium; TS = transseptal; other abbreviations as in Figures 1 and 2.

PERIPROCEDURAL ECHOCARDIOGRAPHIC ASSESSMENT

During LAA device implantation (10) echocardiography is the most important imaging modality to support fluoroscopy and is of paramount importance to guide transseptal (TS) puncture, to verify catheter and sheath position in the LAA, to aid device delivery and positioning, to confirm adequate LAA sealing, and to detect complications.

FIGURE 6 Positioning of the Delivery Sheath and Device Deployment



(A) A 2D and 3D TEE is used simultaneously (3D enface aspects on top, corresponding X-plane views on the bottom) to monitor the introduction and the position of the delivery sheath into the LAA **(left image; white arrowheads** mark the delivery sheath**)** and **(B)** the positioning of the occlusion device (a first generation LAA plug was implanted in this case; **red arrowheads** mark the first generation LAA plug occluder) (Online Videos 2 and 3). Abbreviations as in Figure 1.

TABLE 3 Criteria of an Appropriate Device Position for Different Endoluminal Devices

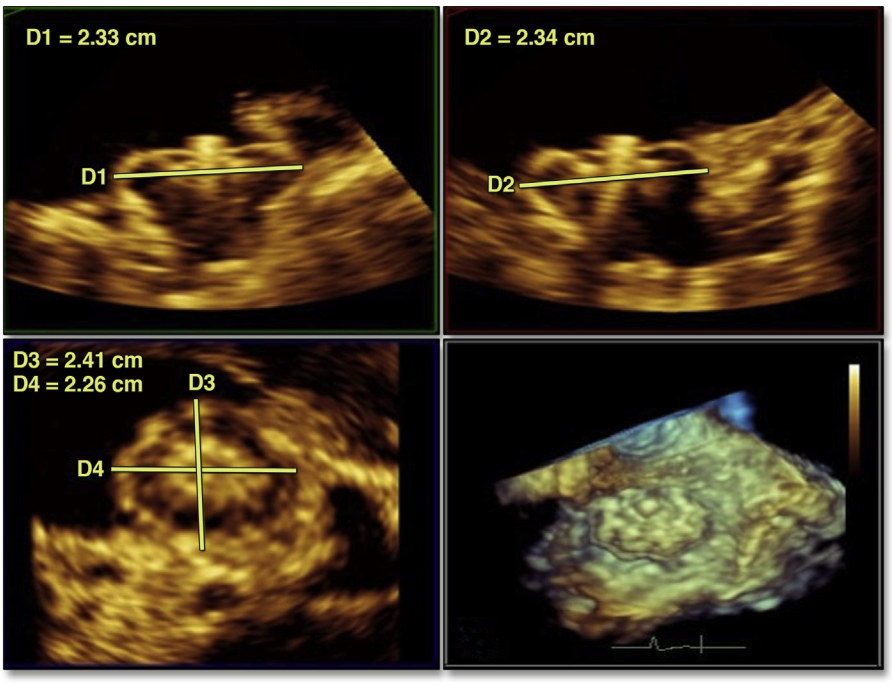
Device	Criteria of an Appropriate Device Position
LAA occluder device	• Position symmetrically in the center of the LAA below the LAA ostium or at the ostial plane • 8%–20% device compression (some recommend a higher grade of compression of 15%–30%) (10) (**Figure 7**) • Fixations barbs should be in contact with the LAA wall • The device should not protrude >4–7 mm beyond the LAA ostium (depending on device size as outlined in the manufacturer's instructions for use)
First generation LAA plug device	• Two-thirds of the lobe should be positioned distal to the circumflex coronary artery • The distal part of the lobe should have the appearance of a flat tent, thus indicating some amount of compression on the lobe • The disc should cover the LAA ostium with a concave appearance • The flexible waist that connects the disc and the lobe should be clearly visible • Fixation anchors should be engaged with the LAA wall
Flexible LAA occlusion device	• The hub of the occluder on the left atrial side should be located proximal to the landing zone • The anchors (best visualized in fluoroscopy) should be placed ~5 mm distal to the landing zone • A distal contrast injection provides confidence in device position, stability, and occlusion • Landing zone = distal occluder margin

Abbreviations as in Tables 1 and 2.

Multiplanar 2D TEE is most commonly used for procedural guidance but intracardiac echocardiography has also been suggested as a feasible alternative imaging solution (62,63). Because the interaction of different moving structures can frequently not be visualized in one single plane, RT 3D TEE facilitates the procedure by providing views where targets (e.g., the LAA), wires, catheters, sheaths, and devices can be observed in one single view and in relation to each other. RT 3D TEE provides more accurate morphological information, facilitates the maneuvering and alignment of devices to the target structures (64), and is recommended for the guidance of LAA closure procedures (65).

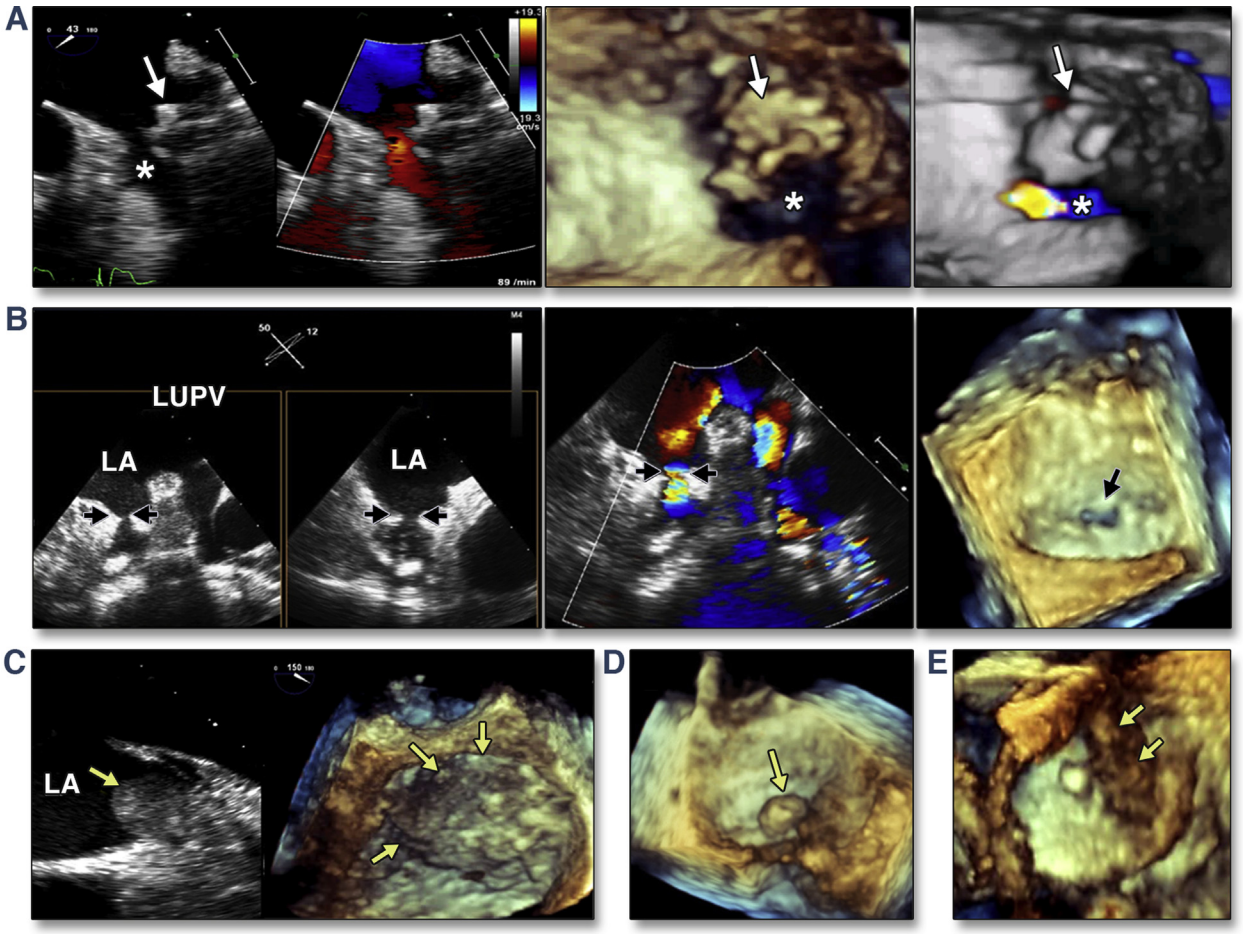
Regardless of the device type chosen to occlude the LAA, procedural steps with regard to transcatheter endoluminal LAA closure are similar. The procedure is optimally guided using 2D and 3D TEE in combination. Before the TS puncture LAA clot formation has to be excluded once more, the LAA morphology should be reassessed, and LAA

FIGURE 7 Measurement of Device Compression After Implantation of a 27-mm LAA Occluder Device



This 3D reconstruction gives an example of the measurement of the device compression. The device diameter after device implantation is measured in different planes: 45°, **upper panel left side** (D1 = 2.33 cm); 135°, **upper panel right side** (D2 = 2.34 cm); corresponding enface measurements, **bottom left side** (D3 = 2.41 cm; D4 = 2.26 cm). The image on the **bottom right side** provides a 3D enface view. In this case the measured compression is 11% to 16% and therefore in the target range (8% to 20% = 84% to 89% of the original device size). Abbreviation as in Figure 1.

FIGURE 8 Complications



(A) Highly compressed LAA occluder device **(white arrows)** is placed in 1 deep lobe. Another large lobe is completely uncovered **(white asterisk)**. This situation is shown using 2D TEE **(left)** with and without color Doppler and an enface 3D TEE image without **(middle)** and with **(right)** color Doppler. **(B)** Unsuccessful LAA ligation using a LAA ligation device. A partially closed LAA is seen by using TEE X-plane imaging **(left)** and color Doppler demonstrating flow coming in and out **(middle)** and by using a 3D enface view from the left atrial side **(right)**; the **black arrows** mark the residual leak at the level of the suture ligation. **(C–E)** Thrombus formation on different devices **(marked with yellow arrows)** by using TEE during follow-up (**C** = LAA occluder device in a 2D TEE plane and a 3D TEE enface view; **D** = LAA ligation device suture occlusion in a 3D TEE enface view; **E** = first generation LAA plug in a 3D TEE enface view). Abbreviations as in Figure 1.

dimension measurements are repeated and combined with angiographic measurements to select the most suitable device type and an appropriately sized device. As illustrated in **Figures 5 and 6** the following procedural steps have to be monitored: TS puncture (Online Video 1), positioning of the delivery sheath in the LAA (Online Video 2), and device deployment (Online Video 3).

ASSESSMENT OF DEVICE POSITION IMMEDIATELY POST-PROCEDURE. Complete occlusion of the LAA and the absence of any alteration of surrounding structures (left upper pulmonary vein or mitral valve) should be confirmed immediately after implantation by the use of fluoroscopy and 2D and 3D TEE (**Figure 1**). Color-flow Doppler using a low Nyquist limit is used to assess if there is incomplete LAA occlusion and a persistent communication between the LAA cavity and the LA. In some patients complete closure cannot be achieved and a peridevice gap may occur with any of the currently available devices (13,17,19,20,66–68).

There is no consensus as to what constitutes a significant peridevice leak after LAA device occlusion. Because there are data for noninferiority in patients with a residual leak with a jet size ≤5 mm after implantation of a LAA occluder device compared with warfarin therapy in the PROTECT-AF trial

TABLE 4 Specific Complications During LAA Closure, Their Mechanisms, Incidences, and Prevention/Treatment Options

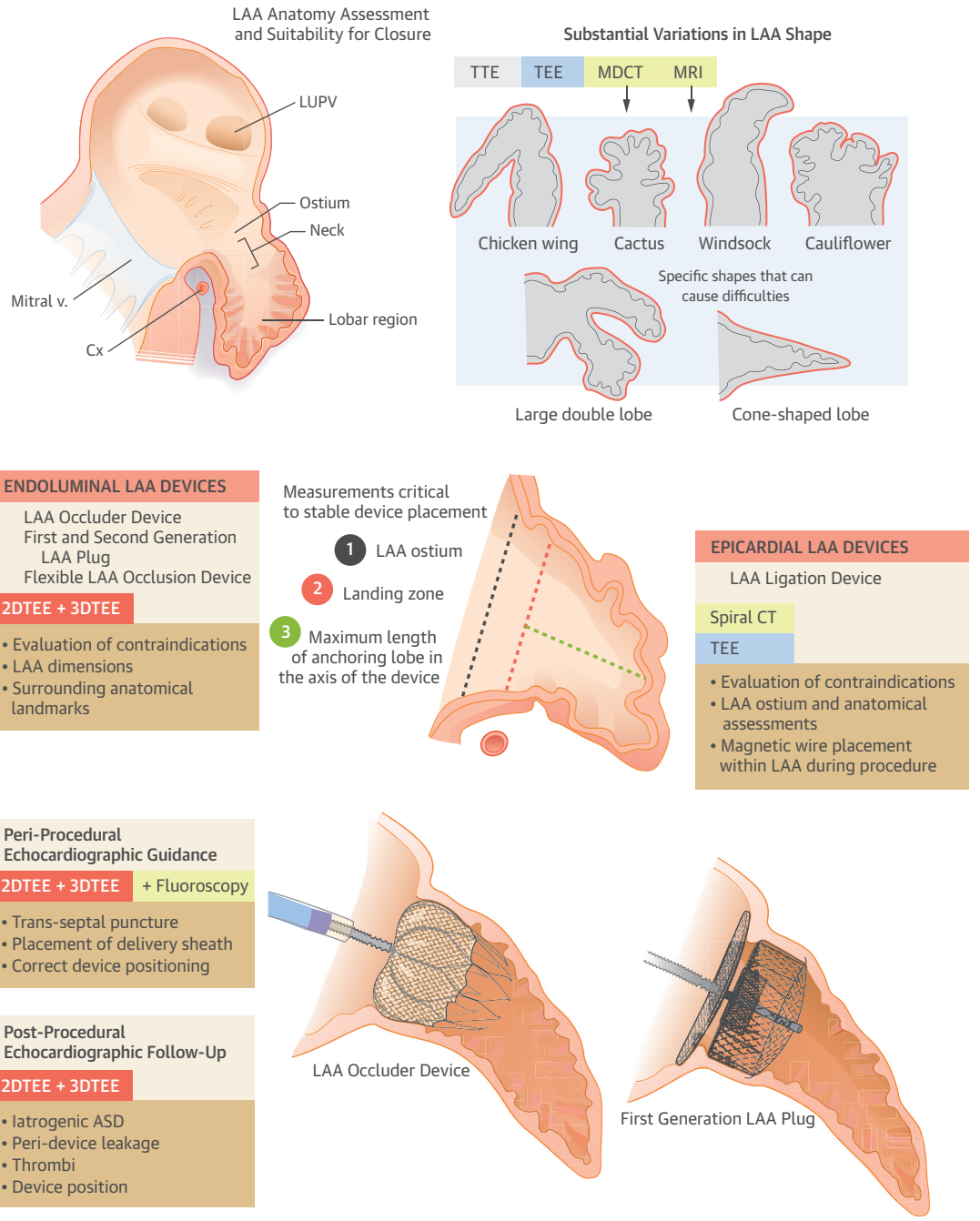
Complication	Mechanism	Incidence	Treatment/Prevention
Pericardial effusion/tamponade	Perforation of the LA or LAA by wires, catheters, devices Incorrect transseptal puncture	LAA occluder device: serious pericardial effusion, up to 5.2% (PROTECT-AF) (5,11) First generation LAA plug: pericardial effusion or tamponade in-hospital, 1.24%–3.5% (14) Flexible LAA occlusion device: 2.7% up to a 45-day FU (19) LAA ligation device: significant periprocedural pericardial effusion, 3.7%–10.4% (22,23) Periprocedural tamponade, 4.5% (23)	Pericardial drainage Surgery if needed
Device embolization	Incorrect sizing, incorrect device deployment	LAA occluder device: 0.0%–2.7% (5,11) First generation LAA plug: in-hospital, 0.21%–1.4% (14,16); at FU, 0% (13,15,16) Flexible LAA occlusion device: 0% up to 45 days FU (19)	Transcatheter removal (e.g., by the use of snares) Surgery if needed
Thrombus formation on the device or at the closure site	Exposure of foreign material	LAA occluder device: 4.2% (PROTECT-AF) (5,11) First generation LAA plug: up to 14% (13) Flexible LAA occlusion device: 0% up to 45 days FU (19) LAA ligation device: 4.8% (median FU, 122 days) (23)	Anticoagulation therapy
Residual flow into the LAA	Incomplete coverage of the LAA	LAA occluder device: 8% of patients had a residual leak >5 mm at 6-month FU (5) Residual leaks intraprocedural: 27.6%; 29.3% at 45-day FU, and 34.5% at 1 year (67) 32.0% of implanted patients had at least some degree of peridevice flow at 12 months (68) First generation LAA plug: 16.2% mild peridevice leakage at 6 months FU; 2.4% flow >3 mm color jet (16) Flexible LAA occlusion device: after 45 days post-implant 3% of patients had a residual leak >3mm (19) LAA ligation device: after the procedure, residual leak <5 mm 8%; >5 mm 0% (complete closure, 92%) (23); at median FU of 122 days, residual leak ≥5 mm 6%, <5 mm 14%, complete closure 79% (23)	Accurate sizing and assessment of morphology pre-procedure
Persistent ASD	Transseptal sheath placement	11% of patients had a persistent ASD at 6-month and 7% at 12-month FU (71)	The iatrogenic ASDs are usually small and do not require treatment
Chest pain/pericarditis	Pericardial irritation, specific for the LAA ligation device procedure caused by pericardial access	Pericarditis: 14% (3/21) (21)	Chest pain usually resolves once the pigtail catheter is removed from the pericardium Pericarditis treatment with colchicine ± NSAIDs
Alteration of the LUPV, the MV apparatus, or the circumflex coronary artery	Because of their close anatomic relationship a device placed in the LAA can theoretically alter the LUPV, causing pulmonary vein stenosis, or even alter the MV apparatus or the circumflex coronary artery	To our knowledge no cases describing one of these potential complications are reported to date	Pulmonary vein anatomy should be assessed by 2- and 3-dimensional TEE and pulmonary vein flow should be evaluated by the use of color flow and pulse wave Doppler. A pre- and post-procedural evaluation should also include a detailed assessment of the MV anatomy and grading of mitral regurgitation severity if present Repeated ECGs should also be obtained

ECG = electrocardiogram; FU = follow-up; NSAID = nonsteroidal anti-inflammatory drug; other abbreviations as in Tables 1 and 2.

(the jet-diameter was measured by 2D TEE with color Doppler in multiple planes; however, absence of a specified Nyquist limit represents a limitation) (5), a peridevice leak ≤5 mm seems to be acceptable and not associated with an increased thromboembolic stroke risk.

Correct device position is of major importance. If an endoluminally implanted occlusion device

CENTRAL ILLUSTRATION **Imaging Approach to LAA Closure: An Overview**



Top left panel shows a cross section of the left atrium and the orientation of the LAA, left circumflex coronary artery, mitral valve as well as the left upper pulmonary vein. Top right panel depicts the various LAA morphologies and shapes. Middle panel demonstrates the critical locations where measurements need to be made for optimal sizing of the LAA occlusion device. Bottom left panel illustrates the optimal placement of LAA occluder device and first generation LAA plug for LAA occlusion. ASD = atrial septal defect; CT = computed tomography; Cx = circumflex coronary artery; LAA = left atrial appendage; LUPV = left upper pulmonary vein; MDCT = multidetector computed tomography; MRI = magnetic resonance imaging; TEE = transesophageal echocardiography; TTE = transthoracic echocardiography.

is placed too deep into the LAA, more proximal originating lobes may be uncovered. For cases in which the device is implanted too proximal in the LAA the occluder may not be adequately compressed by the LAA walls and thus be unstable and it can embolize. **Table 3** summarizes criteria for appropriate positioning for different endoluminal devices. A certain amount of device compression is needed with every device. **Figure 7** gives an example of the evaluation of device compression after implantation of an LAA occluder device.

After a device is inserted, but before its release from the catheter, gentle traction on the catheter is applied to the device ("tug" test) to demonstrate that the device positioning is stable. The device and the surrounding tissues should move in unison during the tug test.

DETECTION OF COMPLICATIONS. Complications may occur at any time during the intervention and during patient follow-up. **Figure 8** demonstrates echocardiographic examples of acute and delayed complications of LAA exclusion. The immediate detection of acute complications by echocardiography is of paramount importance to minimize or avoid adverse clinical consequences. **Table 4** provides an overview of potential complications, their mechanism and incidence, and prevention and treatment strategies.

POST-PROCEDURAL ECHOCARDIOGRAPHIC FOLLOW-UP

TTE is recommended after the intervention before the patient is discharged from the hospital to confirm that no relevant device migration occurred and to exclude the development of a pericardial effusion. TEE is often used for standard echocardiographic follow-up at 1, 3, or 6 and 12 months, then annually (when there is no evidence of device migration or complications after 1 year further surveillance can be done annually by using TTE; in case there is an abnormality that needs clarification, TEE should be performed in addition) to reassess the implanted device for a stable position, migration or embolization, erosion, thrombus formation, and peridevice gaps. Echocardiography is also used to monitor for any interference with neighboring structures, such as the mitral valve, left upper pulmonary vein, and the circumflex coronary artery; but to our knowledge no such cases have been reported to date. The formation of a thrombus or fibrosis within the LAA cavity distal to the occlusion device is a normal finding but careful attention is warranted to evaluate newly developed thrombotic clots either attached to the device or within the LA because this would be an indication for anticoagulation therapy.

Complete closure of the LAA represents one of the major determinants of a successful procedure. Nevertheless, the presence of a peridevice leak is a common finding and there are no data at present that demonstrate that it is associated with an increased risk of stroke (67–69).

Notably it has been shown that intraprocedural leaks can become larger over time and persist for more than 1 year, and new peridevice leakages can also occur during follow-up (66). Consequently, it is important for patients to have serial follow-up echocardiograms. Despite there being no definitive data, it is currently recommended (according to the PROTECT-AF data) that anticoagulation therapy should be continued if there is a persistent peridevice gap >5 mm (5). In some patients with a relevant leak resulting from an uncovered lobe the implantation of a second device is an option to complete LAA closure (70).

During each follow-up atrial septal defect secondary to the TS puncture should be reassessed by the use of TEE (2D or 3D) with and without color Doppler. Saline contrast injections along with a Valsalva maneuver are useful to identify the presence of a right-to-left shunt. These iatrogenic atrial septal defects have a high spontaneous closure rate over time. In one study, only 11% of patients had a persistent atrial septal defect at 6 months and 7% at 12 months after the procedure. Moreover, to date, residual atrial septal defects have not been associated with an increased rate of stroke or systemic embolization during long-term follow-up (71).

CONCLUSIONS

LAA device closure is a relatively new, but evolving treatment strategy to prevent embolic events in patients suffering with nonvalvular AF. Echocardiography, using both 2D and 3D TEE, currently represents the most important imaging tool to assess the suitability of the LAA anatomy for the procedure, for selecting the optimal device types and sizes, for guiding the LAA closure procedure in conjunction with fluoroscopy, and for follow-up imaging after device implantation.

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