

Echo Essentials for Endoluminal LAA Closure

Echocardiography is the imaging modality of choice for this new interventional technique.

**BY NINA C. WUNDERLICH, MD; MARTIN J. SWAANS, MD; HARALD KÜX, MD;
ROY BEIGEL, MD; AND ROBERT J. SIEGEL, MD, FACC**

Atrial fibrillation (AF) is associated with a high risk of thromboembolic cerebral ischemic events in affected patients. Up to 20% of all strokes are caused by AF.¹⁻³ Thus, stroke prevention is a major concern in the management of this common arrhythmia.

Anticoagulation treatment with either vitamin K antagonists, direct thrombin inhibitors, or factor Xa inhibitors has shown to be effective in reducing thromboembolism and in preventing stroke in patients with AF.⁴⁻¹¹ However, all of these agents have the potential to increase the patient's risk of bleeding.¹² Consequently, AF management in daily practice remains challenging.¹³

Additionally, many patients cannot be treated with anticoagulation due to contraindications.¹⁴ More than 60% of patients with an indication for anticoagulation therapy are untreated.^{15,16} Due to the limitations and complications of anticoagulation therapy, interest in percutaneous left atrial appendage (LAA) closure has become appealing. Because more than 90% of thrombi in patients with nonvalvular AF form in the LAA,^{17,18} it seems reasonable to exclude this major source of thrombus development from the systemic circulation.

The percutaneous left atrial appendage transcatheter occlusion (PLAATO) occluder (Boston Scientific Corporation, Natick, MA) was the first percutaneous

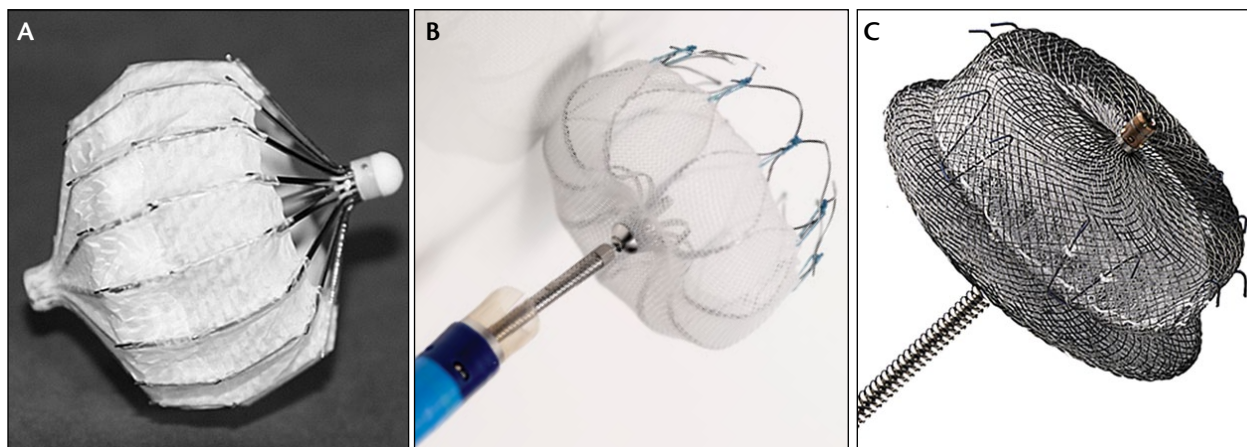


Figure 1. Three different endoluminal LAA occlusion devices. The PLAATO device (© 2014 Boston Scientific Corporation or its affiliates. All rights reserved. Used with permission of Boston Scientific Corporation) consists of a self-expandable nitinol cage (18–32 mm in diameter) and is coated with expanded polytetrafluoroethylene (A). The Watchman device (© 2014 Boston Scientific Corporation or its affiliates. All rights reserved. Used with permission of Boston Scientific Corporation) consists of a self-expanding nitinol frame covered by a polyethylene terephthalate membrane on the left atrial side. Fixation barbs around the mid-perimeter allow for secure engagement to the LAA wall (available sizes: 21, 24, 27, 30, 33 mm) (B). The Amplatzer cardiac plug device (with permission from St. Jude Medical, Inc.) consists of a proximal disc (to cover the LAA orifice) and a distal lobe (to secure the device in the LAA) connected by a flexible central waist. Six pairs of hooks are attached to the lobe, thus enabling secure engagement to the LAA wall. The proximal discs are 4 mm larger for lobe sizes 16 to 22 mm and 6 mm larger for lobe sizes 24 to 30 mm (available sizes: 16, 18, 20, 22, 24, 26, 28, 30 mm) (C).

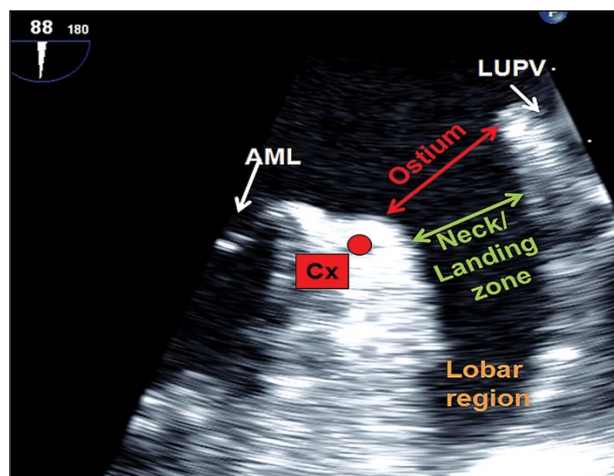


Figure 2. LAA regions and the relationship to surrounding structures. In this 2D TEE image (88°), the different LAA regions (ostium, neck, lobar region) are shown. The close relationship between the LAA ostium and the LUPV and MV can be appreciated. The neck, where the device landing zone is located, shows a close relationship to the circumflex coronary artery (Cx). AML indicates anterior mitral leaflet.

device that was specifically designed for LAA occlusion (Figure 1A). It was first implanted in August 2001 (note, it is no longer available) and was subsequently followed by the Watchman device (Boston Scientific Corporation, Natick, MA) (Figure 1B) and the Amplatzer cardiac plug (St. Jude Medical, Inc., St. Paul, MN) (Figure 1C). The Amplatzer cardiac plug and the Watchman closure devices have the most clinical experience and published data to date. Current trials with these devices demonstrate that LAA closure with endoluminal devices is effective in reducing thromboembolic cerebral events.¹⁹⁻²⁵

Transesophageal echocardiography (TEE) is the main imaging modality used in assessing anatomic LAA variations to select an appropriate device, guiding the procedure, evaluating the final device position, and monitoring the occurrence of complications. In this article, we focus on current echocardiographic imaging approaches for the selection of suitable patients for endoluminal LAA device closure with the most commonly used devices (Watchman occluder and Amplatzer cardiac plug) and the periprocedural imaging aspects of LAA device delivery.

PREPROCEDURAL ECHOCARDIOGRAPHIC ASSESSMENT

Before a planned LAA closure procedure, two-dimensional (2D) and three-dimensional (3D) transthoracic echocardiography (TTE) allow for the analysis of left ventricular function, left atrial (LA) dimensions, and the

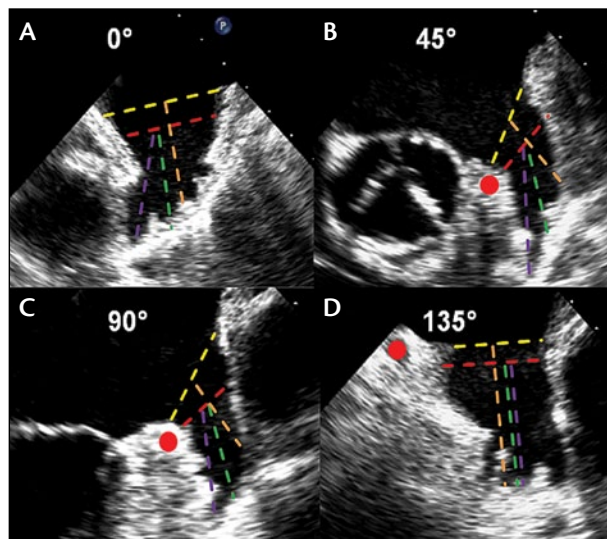


Figure 3. LAA measurements in different 2D TEE views; 2D TEE measurements are usually performed in four different mid-esophageal views: a four-chamber view (~ 0°) (A), a short-axis view at the base (~ 45°) (B), a two-chamber view at approximately 90° (C), and a long-axis view at approximately 135° (D). The colored lines illustrate the different measurements needed before device closure. The yellow line demarcates the LAA ostial plane. With an Amplatzer device, a second measurement is required approximately 10 mm into the LAA parallel to the ostial plane in the axis of the neck (light orange line) to determine the landing zone of the stabilizing lobe. A depth of ≥ 10 mm within the LAA is required. The depth is measured along the axis of the neck perpendicular to the ostial plane (light orange line). The red line represents the landing zone of a Watchman device. This measurement is obtained from the inferior part of the LAA ostium at the level of the circumflex coronary artery (marked by a red dot; alternatively, the level of the anterior MV leaflet can be chosen as a landmark) to a point 1 to 2 cm distal to the tip of the rim to the LUPV. The depth should be measured perpendicular to the landing zone measurement, as the axis of the device will orientate in this direction. The purple line marks the total length of the LAA.

exclusion of contraindications or unfavorable conditions, such as mitral stenosis, significant valve disease requiring surgery, or the need for permanent oral anticoagulation due to other reasons (eg, in patients after a mechanical valve replacement or in patients who are experiencing thrombus in the left ventricle). Because the LAA cannot be adequately assessed by TTE, TEE is requisite. Active endocarditis and LAA thrombi must be excluded prior to the procedure. In situations where there is uncertainty about the presence of LAA thrombus, the use of an ultrasound contrast agent during TEE often improves atrial thrombus detection in patients with AF.²⁶ If a thrombus

is detected, it is recommended to treat the patient with oral anticoagulants until the thrombus has resolved.

Another major indication for the use of TEE is to obtain a detailed morphologic assessment of the LAA due to the possible considerable anatomic variation in the LAA. There are enormous variations in the LAA shape (most commonly, the LAA is bent or spiral in shape), orifice diameters (10–40 mm), length (16–51 mm), volumes (0.7–19.2 mL), and number of lobes (> 50% of LAAs have more than two lobes).²⁷ Therefore, it is crucial to have adequate visualization of the anatomic LAA characteristics in every single patient prior to percutaneously occluding the LAA in order to avoid complications.

A multiplane, 2D TEE analysis from 0° to 180° improves the evaluation of the frequently complex LAA morphology,²⁸ and 3D TEE has been shown to add even more valuable information by allowing for a more detailed visualization and quantitative analysis of the LAA orifice area.²⁹

To characterize the LAA with regard to device closure and to improve communication between the interventionist and the echocardiographer by clarifying the nomenclature, it is easiest to divide the LAA into three regions:

1. The ostium represents the opening to the left atrium. The shape of the ostium is consistently elliptical rather than round,³⁰ and a close relationship to the mitral valve (MV) and the left upper pulmonary vein (LUPV) has to be taken into consideration (Figure 2).
2. The neck can be described as a consistent, narrow junction with the body of the left atrium. The landing zone of endoluminally implanted devices is localized in this region. The neck of the LAA is in a close relationship to the circumflex coronary artery (Figure 2).
3. The lobar region is the largest and most variable distal part of the LAA (Figure 2). Different morphologies were recently used to categorize this region of the LAA (windsock, cactus, cauliflower, and chicken wing).³¹ A clear correlation between these different LAA morphologies and stroke risk could not be demonstrated, but the extent of LAA trabeculations (cauliflower morphologies) had more trabeculations than chicken wing morphologies, and smaller LAA orifice diameters were associated with prevalent stroke.^{31,32}

LAA Measurements

All measurements needed to characterize the LAA before closure should be performed at the end of diastole when LAA diameters and volumes are largest and with normal LA filling pressures (> 10 mm Hg) to avoid undersizing. Multiple echocardiographic measurements in multiple views are made in addition to fluoroscopic evaluation to accurately define ostial diameter, landing

Precise knowledge of the dimensions of the landing zone is particularly important in selecting the appropriate device size.

zone diameter, angle, and depth, as well as the number and origin of lobes of the LAA.

When 2D TEE is used for sizing, measurements must be performed in multiple planes. Usually, the required diameters are measured in four different midesophageal views: (1) in a four-chamber view (0°–20°), (2) in a 45° to 60° view at the level of the aortic valve, (3) in an apical two-chamber view at approximately 90°, and (4) in a long axis view (120°–135°) (Figure 3). Slight rotations of the probe are often useful to depict additional lobes.

Because there are limitations to 2D imaging in characterizing complex 3D morphologies, it has been found that real-time 3D TEE–derived measurements of LAA dimensions are more closely related with CT measurements than 2D TEE measurements. Consequently, 3D measurements are preferred when available (Figure 4).³³

Precise knowledge of the dimensions of the landing zone is particularly important in selecting the appropriate device size. To ensure proper device engagement with the LAA wall and to guarantee stable and safe device positioning, the device size is usually chosen to be a few millimeters larger (according to the instructions for use for the different device types) than the measured appendage diameters. This oversizing results in the appendage wall securing the device by compression forces. Undersizing carries the potential risk of device migration or even embolization. Significant oversizing should also be avoided because it may lead to cardiac perforation, pericardial effusion, and cardiac tamponade.^{34–36} Additionally, the maximum length of the main lobe has to be measured in the expected axis of the device to ensure that the LAA can accommodate the selected occluder.

For the Amplatzer device, the landing zone in the anchoring lobe is measured at approximately 10 mm distal from the ostial plane into the lobe. The depth has to be measured in the axis of the neck (nearly perpendicular to the ostial plane). An LAA depth of ≥ 10 mm and an LAA width ≤ 28 mm is required to place the Amplatzer device safely into the LAA. Measurement of the landing zone for the Watchman device should be performed from the inferior part of the LAA ostium at the level of the circumflex coronary artery to a point 1 to 2 cm distal to the tip of the rim to the LUPV (ligament of Marshall). An LAA width of

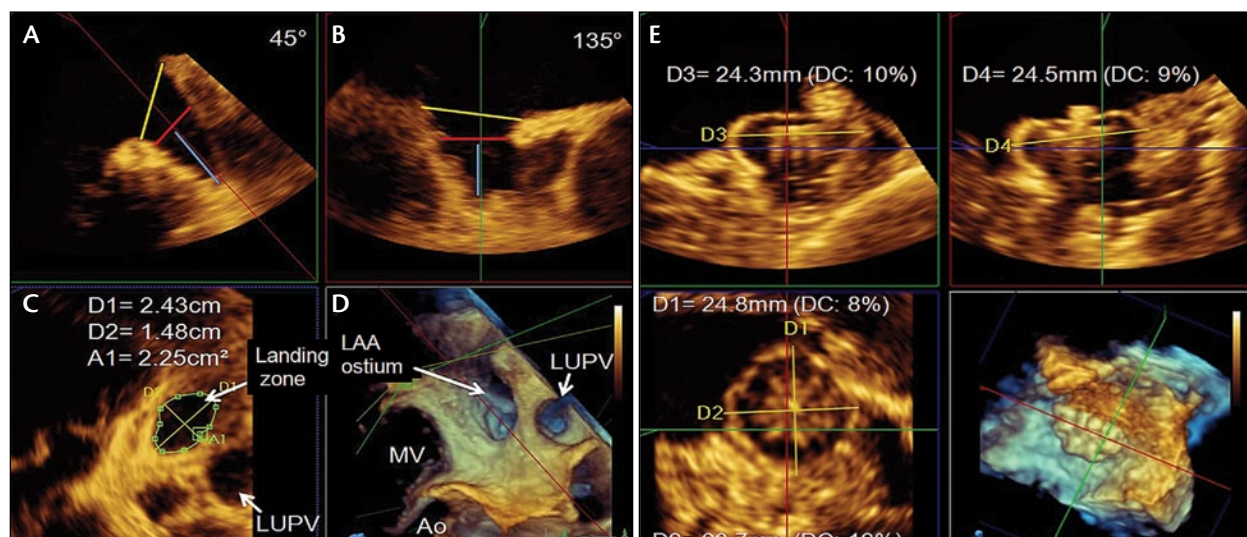


Figure 4. Three-dimensional measurements in a postprocessing analysis: 45° (A) and 135° (B) x-plane TEE images are shown. The yellow line demarcates the LAA ostium. The red line illustrates the measurement of the landing zone (for a Watchman device), and along the blue line, the depth of the LAA is measured. The long-axis view (B) reveals a chicken-wing morphology. An enface plane (z plane) at the level of the landing zone is provided, and the diameters and area are measured (C). In a 3D enface view, the close relationship of the LUPV, the LAA ostium, and the MV can be appreciated (D). According to the largest measurement of 24.3 mm (C), a 27-mm Watchman device was selected. The compression of the device is measured after placement in different planes (8%–12% in this case) (E). The appearance of the 27-mm Watchman device can be appreciated in an enface 3D view (right lower panel). Ao indicates aortic valve; DC, device compression.

17 to 31 mm is required. The LAA depth is measured perpendicular to the measured landing zone and has to be ≥ 19 mm for the smallest device size (21 mm).

Because some anatomic variations are more challenging for endoluminal device closure than others, they should be evaluated in advance to plan the procedure. A secondary lobe originating close to the ostium can complicate the procedure, resulting in a lobe that may stay unsealed after device positioning; this is true especially when a Watchman device is used. Two lobes of nearly the same size, separated by a large rim in between them, may also cause technical problems when the proximal part is too short to allow safe device placement. The presence of a chicken-wing morphology (Figure 4B and 4E [upper right panel]) with an early (< 20 mm from the ostium) and severe bend ($< 180^\circ$) constitutes one of the most difficult anatomic settings for percutaneous LAA closure. Specific implantation strategies may be necessary to successfully close such a morphology.³⁷

A device placed in the LAA can theoretically compress the LUPV or alter the MV apparatus due to a close anatomic relationship between the structures (Figure 4D). Therefore, pulmonary vein anatomy and vein flow should both be evaluated by color flow and pulse wave Doppler. Similarly, the MV anatomy, as well as the severity of mitral regurgitation, should be assessed in detail before and after the procedure.^{38,39}

PERIPROCEDURAL ECHOCARDIOGRAPHIC ASSESSMENT

Echocardiography is the most important imaging modality to support fluoroscopy during LAA device implantation and is essential to aid device delivery and positioning and to monitor complications. Because multiplanar 2D TEE imaging has been widely adopted, it is currently the echocardiographic modality of choice to guide the procedure. Intracardiac echocardiography has also been proposed as a viable alternative option.⁴⁰

Three-dimensional echocardiography (particularly real-time 3D TEE) has recently become an important adjunct in structural heart disease interventions. The interaction of moving targets, such as the LAA, catheters, wires, and devices, is frequently difficult to visualize in one plane. Three-dimensional TEE provides more detailed information about the anatomy, facilitates the manipulation and alignment of devices to the targets,⁴¹ and is therefore an invaluable tool that is recommended for procedural guidance.⁴² Regardless of the specific device selected for LAA closure, procedural aspects related to percutaneous LAA closure are similar. TEE (2D and 3D, if available), or alternatively intracardiac echocardiography, is used to guide the following procedural steps.

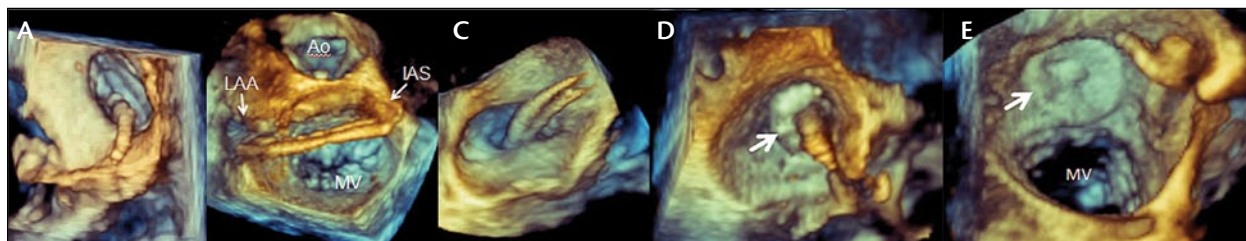


Figure 5. Monitoring of the procedural steps by 3D TEE. The 3D TEE enface view (A). A wire can be seen placed in the LAA. A wide-angle acquisition shows the delivery sheath crossing the interatrial septum (B). The tip is placed in the LAA. The entire part of the delivery sheath in the left atrium can be seen, and the relation to surrounding structures can be precisely evaluated. In an enface 3D TEE view, the delivery sheath is shown in the LAA (C). The positioning of a Watchman device (white arrow) can be seen, with the device still attached to the delivery cable (D). An example of a released Amplatzer device (white arrow; E). The wide-angle acquisition allows for an adequate assessment of interferences with neighboring structures, such as the MV. Ao indicates aortic valve; IAS, interatrial septum.

Reassessment of LAA Diameters and Anatomy

Once thrombus formation in the LA or LAA has been excluded, the size and the endoluminal LAA anatomy should be reassessed prior to the procedure and combined with fluoroscopic measurements to choose an appropriate device type and size.

Transseptal Puncture

Echocardiography is of major value in determining the preferred puncture site in the interatrial septum. A short-axis view at the base in 2D TEE imaging ($\sim 45^\circ$) allows for orientation in an anteroposterior direction, and a long-axis view (90° – 120° = bicaval view) provides orientation in the cranial and caudal directions. Three-dimensional x-plane allows imaging in a short-axis view at the base and a bicaval view simultaneously, thus facilitating transseptal (TS) puncture. The TS puncture site is important to allow for coaxial entry into the LAA and is dependent on the origin and the course of the LAA, the shape of the delivery sheath, and the particular device to be implanted. In general, the TS puncture site is ideally slightly more inferior when an Amplatzer device is chosen than that used for the Watchman device.

Positioning of the Delivery Sheath in the LAA

Once access to the LA is achieved, a sheath is advanced into the LA, and a pigtail catheter is inserted into the LAA over a soft wire (Figure 5A). This technique minimizes the risk of LAA perforation. Echocardiography is used to monitor the introduction and the position of the delivery sheath into the LAA (Figure 5B and 5C).

Device Deployment

The selected device is then inserted, and the device is deployed by retracting the delivery sheath (Figure 5D and 5E). The orientation of the device to the LAA and

LA should be assessed. The axis of the device should be in alignment with either the neck (with the use of an Amplatzer device) or the major axis of the LAA (with the use of a Watchman device).

Assessment of the Final Device Position and Result

Several fluoroscopic and echocardiographic parameters are used to determine a correct and stable device position. Complete coverage of the LAA should be assessed, and any interference with neighboring structures (such as the LUPV or the MV) has to be noted. Color-flow Doppler with a low Nyquist limit should be used to assess for peridevice leakage and persistence of communication between the LA and LAA (Figure 6A). There is an incidence of leakage of up to 16.2% with the Amplatzer device^{43–45} and up to 35% within the first year after implantation of a Watchman device (Figure 6A, 6B, 6D, and 6F).^{46,47} A uniform definition of residual leakage after LAA device closure does not exist at the moment,^{20,24} but in the PROTECT-AF trial, patients with a residual communication < 5 mm after placement of a Watchman device, as measured on 2D TEE, were spared anticoagulation therapy. In these patients, there was noninferiority compared with anticoagulation therapy in the device group.^{23,24} Therefore, a residual leak ≤ 5 mm appears to be acceptable and not associated with an increased risk of stroke. Patients with residual peridevice leaks > 5 mm have to stay on anticoagulation therapy. In patients with relevant residual peridevice leakage resulting from uncovered lobes, an additional interventional procedure to cover unsealed lobes with a second device may be considered.⁴⁸

Watchman devices have to be implanted so that the device is positioned below the LAA ostium or at the ostial plane. A device that is implanted too deep into the LAA carries the potential risk that more proximally locat-

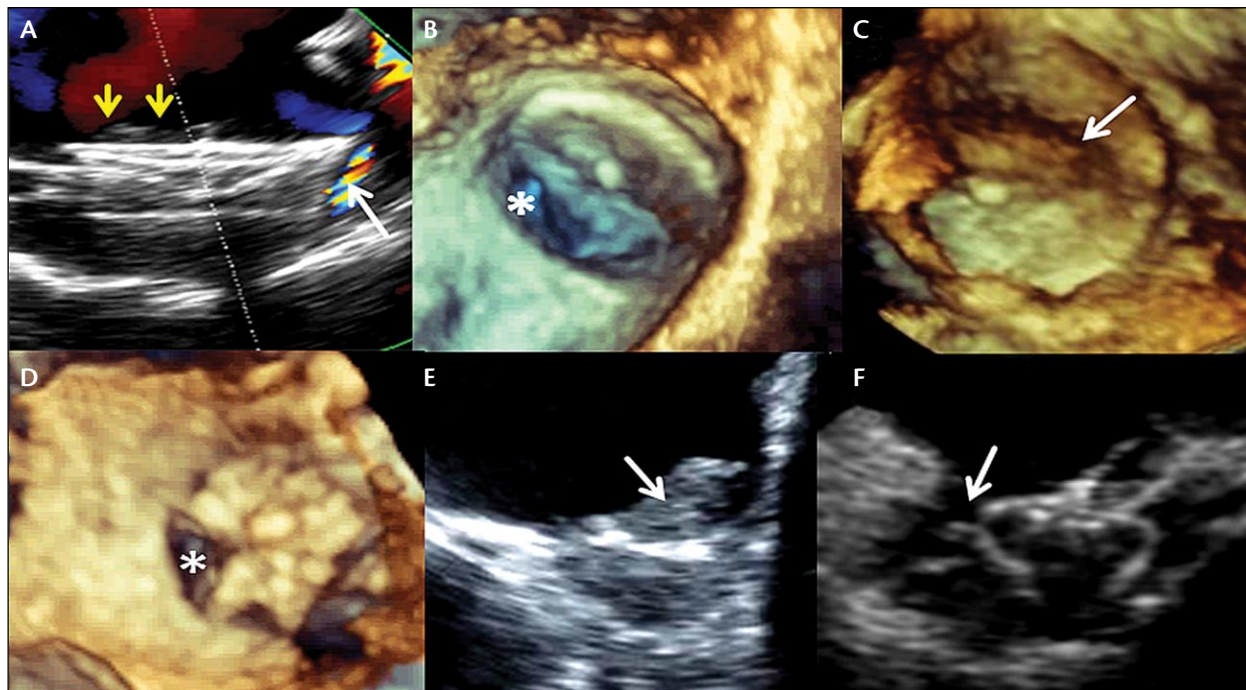


Figure 6. Two-dimensional TEE color Doppler showing peridevice leakage (white arrow; A). In addition, a small thrombus was detected on the left atrial side of the Amplatzer disc (yellow arrows). A 3D TEE enface view from the left atrium demonstrating incomplete coverage by an Amplatzer occluder (B). The disc of the Amplatzer device sits oblique in the LAA ostium. A proximal lobe remains unsealed (white asterisk). An enface 3D TEE image demonstrating a thrombotic mass on the left atrial side of the disc of the Amplatzer device (C). A 3D TEE enface view shows an example in which a Watchman occluder is placed (D). The white asterisk marks a secondary lobe that originates very proximal. This lobe is uncovered. A 2D TEE view (125°) showing thrombus formation on a Watchman device (E). A 2D TEE image at 135° in which a Watchman occluder can be detected and is implanted too deep (F). A relevant gap persists (white arrow). The LAA has a chicken wing appearance.

ed lobes are not covered (Figure 6F), and a device that is implanted too high (protruding out of the LAA) may not be stable. The fixation anchors should be engaged with the LAA wall, and device compression of 8% to 20% of the original device size should be achieved (Figure 4E). After device deployment, but before its release from the catheter, gentle pulling on the catheter is applied to the device (tug test) to confirm that the device is in a stable position.

Specific device release criteria for the Amplatzer occluder include that the distal part of the lobe should have a convex, tent-like appearance (tenting), thus indicating some compression on the lobe. The disc should seal the LAA ostium completely with a concave appearance, and the waist in between the disc and the lobe should be clearly separated. Also, the lower end of the lobe should be positioned distal to the circumflex coronary artery, which is easily presentable on 2D TEE imaging, and the fixation anchors of the lobe should be engaged with the LAA wall. A stable position may also be confirmed by a gentle tug test. Once a correct and stable device position is confirmed, the device is released.

Assessment of Complications

Complications may occur at any time during the procedure, and their detection by echocardiography is of major importance. The most serious complication is the development of a cardiac tamponade, which may happen due to an incorrect TS puncture or manipulation of catheters, guidewires, or devices in the LA or the LAA, leading to injuries of the left atrial or LAA wall (incidence: 4.8% of patients in the PROTECT-AF trial, and < 2% in the CAP registry due to increased operator experience³⁶; 3.5% of patients who received an Amplatzer device had cardiac tamponade, as described in the initial European experience²⁵).

Another potential complication is the detachment of undetected thrombotic material adherent to the LA wall or LAA by catheter or guidewire maneuvers. Thrombus formation on the device itself is reported to occur in up to 4.2% in patients with use of a Watchman device^{36,49} and in up to 14% (this high incidence was found in a single-center experience) when an Amplatzer occluder was implanted (Figure 6C and 6E).^{43,44} In the

Although LAA closure is a relatively new interventional technique, its use is rapidly expanding worldwide.

ASAP trial, only 0.7% of patients with a device thrombus had an ischemic stroke.⁴⁹ Device embolization was described in 0.6% of the patients in the PROTECT-AF trial³⁶ and in 1.5% of patients when an Amplatzer device was implanted.²⁵ Recent data from a multicenter experience showed a lower rate of device embolization in only 0.21% of patients.⁵⁰ The interatrial septal defects that persist in some patients after TS access are usually small and do not appear to be hemodynamically relevant.

POSTPROCEDURAL ECHOCARDIOGRAPHIC ASSESSMENT

Prior to discharge, TTE is recommended to confirm an unchanged device position and to exclude pericardial effusion or thrombus formation. Echocardiographic follow-up using TEE is reasonable at 1, 3 and/or 6, and 12 months after the procedure. When there is no evidence of device migration or complications, further surveillance can be performed annually with TTE. If there is an abnormality that needs clarification, TEE should also be performed.

The implanted device should be assessed for a stable and unchanged position over time. Embolization, device migration, erosion, and interference with any surrounding structures, particularly the MV and the LUPV (to our knowledge, there is not a single case report describing an alteration of the MV or the LUPV to date, but a theoretical risk persists), have to be noted. Thrombus formation/fibrosis within the LAA is normal to find, but meticulous care is needed to evaluate thrombus formation either on the device or in the LA, as this may necessitate further anticoagulation therapy. In this context, the use of echocontrast agents may be helpful.

The absence of peridevice leakage represents one of the major determinants of successful device closure. Interestingly, it has been shown that leaks may be detected up to 45 days after implantation,⁴⁵ thus indicating that it is essential to continuously focus on the detection of these leaks. In addition, the interatrial septum should be reassessed during each follow-up for persistence of iatrogenic atrial septal defects.

CONCLUSION

Although LAA closure is a relatively new interventional technique, its use is rapidly expanding worldwide. Echocardiography (mainly 2D and 3D TEE) is currently the imaging modality of choice to support an adequate understanding of indications, patient selection, LAA closure procedures, and assessment of results and complications. Adequate knowledge about the use of echocardiography in this context is therefore of paramount importance. ■

Nina C. Wunderlich, MD, is with the Cardiovascular Center Darmstadt in Darmstadt, Germany. She stated that she has no financial interests related to this article. Dr. Wunderlich may be reached at +49-6151-2976-0; wunderlich@kardio-darmstadt.de.

Martin J. Swaans, MD, is with St. Antonius Hospital, Department of Cardiology in Nieuwegein, The Netherlands. He has disclosed that he is a proctor for Boston Scientific Corporation.

Harald Küx, MD, is with the Cardiovascular Center Darmstadt in Darmstadt, Germany. He stated that he has no financial interests related to this article.

Roy Beigel, MD, is with The Heart Institute, Cedars-Sinai Medical Center in Los Angeles, California, and The Heart Institute, Sheba Medical Center, Tel-Hashomer, and the Sackler School of Medicine, Tel Aviv University in Tel Aviv, Israel. He stated that he has no financial interests related to this article.

Robert J. Siegel, MD, FACC, is with The Heart Institute, Cedars-Sinai Medical Center in Los Angeles, California. He stated that he has no financial interests related to this article.

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