STATE-OF-THE-ART REVIEW

Percutaneous Left Atrial Appendage Closure
Procedural Techniques and Outcomes

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ABSTRACT

Percutaneous left atrial appendage closure technology for stroke prevention in patients with atrial fibrillation has significantly advanced in the past 2 decades. Several devices are under clinical investigation, and a few have already received Conformité Européenne (CE)-mark approval and are available in many countries. The WATCHMAN device (Boston Scientific, Natick, Massachusetts) has the most supportive data and is under evaluation by the U.S. Food and Drug Administration for warfarin-eligible patients. The Amplatzer Cardiac Plug (St. Jude Medical, Plymouth, Minnesota) has a large real-world experience over the past 5 years, and a randomized trial comparing Amplatzer Cardiac Plug with the WATCHMAN device is anticipated in the near future. The Lariat procedure (SentreHEART Inc., Redwood City, California) has also gained interest lately, but early studies were concerning for high rates of serious pericardial effusion and major bleeding. The current real-world experience predominantly involves patients who are not long-term anticoagulation candidates or who are perceived to have high bleeding risks. This pattern of practice is expected to change when the U.S. Food and Drug Administration approves the WATCHMAN device for warfarin-eligible patients. This paper reviews in depth the procedural techniques, safety, and outcomes of the current leading devices. (J Am Coll Cardiol Intv 2014;7:1205–20) © 2014 by the American College of Cardiology Foundation.

Atrial fibrillation (AF) is estimated to affect 1.5% to 2% of the general population, and the prevalence is projected to increase to 12.1 million by 2030 in the United States (1). Unfortunately, AF is a major cause of stroke, increasing ischemic stroke risk by 5-fold, and is responsible for 15% of all strokes and 30% of strokes in patients age >80 years (2,3). Strokes associated with AF are also more severe, with victims having a 50% greater likelihood of becoming disabled or handicapped and >50% likelihood of death (4,5). Accordingly, stroke prevention with anticoagulation is among the main pillars of AF management, and anticoagulation guidelines have become more stringent. The Canadian Cardiovascular Society recommends anticoagulation for CHADS2 (congestive heart failure history, hypertension, age ≥75 years, diabetes mellitus history, stroke or transient ischemic attack symptoms previously) ≥1 and the European Society of Cardiology recommends it for CHA2DS2-VASc (congestive heart failure, hypertension, age ≥75 years, age 65 to 74 years, diabetes mellitus, stroke/transient ischemic attack/thromboembolism, vascular disease, sex female) ≥1 (6,7).

Several randomized placebo-controlled trials have demonstrated that oral anticoagulation (OAC) is highly effective in preventing thromboembolism with AF, with landmark meta-analysis showing 64% stroke reduction and 26% mortality reduction with warfarin (8,9). However, a significant proportion (30% to 50%) of eligible patients do not receive OAC due to absolute contraindications or perceived risks of bleeding (10). Long-term therapy with warfarin or novel oral anticoagulation (NOAC) is associated with lifetime major
bleeding risks of 2.1% to 3.6% per year in recent clinical trials (11–13). Although intracranial hemorrhage is consistently lower with NOAC, the overall risk of major bleeding is not diminished with dabigatran or rivaroxaban compared with warfarin (12,13). Apixaban was the only agent that reduced major bleeding (11).

Other concerns and contraindications with OAC include patients with renal and liver dysfunctions (for NOAC), high risk of falls, noncompliance, and those requiring dual antiplatelet therapy after stenting. For warfarin, there are additional issues with drug and diet interaction, the need for monitoring, and a narrow therapeutic window with time in therapeutic range of only 50% to 60% (14,15). Even with the relatively well-tolerated NOAC, the proportion of patients discontinuing NOAC during study follow-up was 15% to 25% (11–13). There is also residual stroke risk of 2% to 5% annually despite optimal anticoagulation (16). These challenges have led to device-based therapies for nonvalvular AF.

Transesophageal echocardiography (TEE), autopsy, and surgical reports confirmed that >90% of nonrheumatic AF-related left atrial thrombi were isolated to, or originated from, the left atrial appendage (LAA) (17). Thus, mechanical approaches to exclude the LAA from systemic circulation were explored, and early attempts by surgical removal or ligation of LAA developed over 60 years ago were limited by the invasiveness and by significant rates of incomplete exclusion that were associated with increased stroke risks (18,19). Minimally invasive approaches have been developed over the past 2 decades and can be broadly divided into endocardial and epicardial devices (Table 1). This paper reviews contemporary percutaneous LAA closure, with in-depth discussions of the procedural techniques and clinical outcomes of leading devices.

**INDICATIONS FOR PERCUTANEOUS LAA CLOSURE**

The current indications for percutaneous LAA closure vary geographically. Recently, the European Society of Cardiology implemented a class IIb recommendation for patients with high stroke risk and contraindications to long-term OAC (7). The majority of procedures performed in Europe adhere to this guideline as reported by Tzikas (20). Among ~1,000 LAA closures, 74% were for patients with major bleeding or at high bleeding risk. Other indications included coronary stenting (23%), drug interaction (18%), stroke on warfarin (16%), renal or hepatic disease (13%), labile international normalized ratio (7%), and risk of falls (7%). In Canada, LAA closure is generally restricted to patients with CHADS2 ≥1 and contraindications to long-term OAC, under the Health Canada special access program. In the United States, the Lariat procedure may be performed for patients at high risk for stroke with or without contraindications to OAC, but WATCHMAN may only be implanted under the CAP2 (Continued Access Protocol 2) registry for patients eligible for OAC (up until early 2014), pending U.S. Food and Drug Administration (FDA) approval.

**PLAATO.** The PLAATO (Percutaneous Left Atrial Appendage Transcatheter Occlusion) device (Atritech Inc., Plymouth, Minnesota) was the first percutaneous LAA device manufactured with the first human implant in 2001 (21). It consisted of a self-expanding nitinol cage (diameter 15 to 32 mm) with 3 anchors on each strut to stabilize the occluder. It was covered with nonthrombogenic polytetrafluoroethylene membrane to exclude blood flow into the remaining LAA. The PLAATO feasibility study involved 64 patients with AF and contraindications to OAC; the observed annual stroke risk was much lower than expected based on CHADS2 score (3.8% vs. 6.6%) with 5-year follow-up (22). Despite this promising early result, the device was withdrawn from the market for commercial reasons.

**WATCHMAN.** The second dedicated LAA device to be manufactured was WATCHMAN, which was originally owned by Atritech Inc. (Plymouth, Minnesota) but acquired by Boston Scientific (Natick, Massachusetts) in 2011. The current second-generation WATCHMAN LAA Closure Technology consists of a self-expanding nitinol frame covered with permeable (160 μm) polyethylene terephthalate (PET) membrane (Figure 1). There are 10 active fixation anchors at the nitinol frame perimeter, designed to engage LAA tissue for device stability. The PET membrane covers ~50% of the proximal outer nitinol frame, which blocks thrombus embolization from the LAA and promotes healing and endothelialization. The device’s spherical contour accommodates most LAA anatomy (case example, Figure 2). There are 5 sizes available (Table 2), delivered through dedicated 14-F sheaths with 12-F inner diameter and 75 cm working length. There are 3 dedicated access sheaths: double-curve, single-curve
(Figure 1), and anterior-curve. The standard workhorse is the double-curve sheath (>90% cases), which allows easier access into superiorly directed distal lobes. The fourth-generation device was evaluated in a European registry, and the fifth generation (WATCHMAN FLX) is awaiting first-in-man evaluation. The WATCHMAN device received the Conformité Européène (CE) mark in 2005 and is under FDA evaluation with anticipated approval in early 2015.

**AMPLATZER CARDIAC PLUG.** Early adopters of percutaneous LAA closure in Europe attempted non-dedicated Amplatzer devices after the PLAATO device was discontinued as there was no other option (23,24). However, the incidence of embolization was high (12%), although the efficacy endpoints were similar to dedicated devices for successfully-implanted devices (24). The dedicated Amplatzer Cardiac Plug (ACP) (St. Jude Medical, Plymouth, Minnesota) was specifically designed to occlude the proximal segment of the LAA and is the third LAA device to be manufactured.

ACP consists of self-expanding nitinol mesh forming a lobe and disk, connected by a central articulating waist (Figure 3). The lobe is implanted ~10 mm inside of the LAA orifice and serves as the key anchoring mechanism, supported by 6 pairs of stabilizing wires distally. The disk deployed in the left atrium is pulled under traction against the LAA orifice by the waist connecting to the lobe, which helps to seal the orifice (case example, Figure 4). Both the lobe and disk have polyester mesh that is sewn in by hand. There are 8 sizes according to the lobe dimension, accommodating LAA diameters of 12.6 to 28.5 mm (Figure 3). The second-generation ACP, Amulet (St. Jude Medical), has a wider lobe, longer waist, recessed proximal end screw, and more stabilizing wires. These features improve the stability of Amulet and theoretically may reduce thrombus formation on the atrial side of the device. Amulet also comes in 8 sizes and accommodates larger LAAs (up to 32 mm).

ACP has to be manually loaded onto the delivery cable, but the Amulet comes pre-loaded on the
delivery cable for ease of setup. Currently, the Amulet is undergoing redesign of the delivery system and will be relaunched in late-2014. ACP received the CE mark in December 2008, and Amulet received it in January 2013.

There were 3 ACP/Amulet delivery sheaths available; the workhorse is the TorqVue™ 45° x 45° (>95% of cases), which has a 3-dimensional distal tip, allowing anterior and superior angulation for coaxial positioning at the landing zone. The TVLA1 and TVLA2 sheaths are no longer being manufactured because of lack of demand. The access sheath size varies according to the device size (Figure 3), although some operators routinely use the largest sheath.

**LARIAT.** The catheter-based Lariat (SentreHEART Inc., Redwood City, California) LAA closure is a complex hybrid procedure that requires both an endocardial and epicardial approach. Lariat is FDA-approved (and CE-marked) for suture and knot tying during surgical applications, but not specifically for stroke prevention with AF. There is a recent surge in interest and procedural volume in the United States due to the availability of this device for patients who are not OAC candidates. Lariat consists of a snare with a pre-tied suture that is magnetically guided epicardially over the LAA. There are 3 components: a 15-mm compliant occlusion balloon catheter (EndoCATH); 0.025- and 0.035-inch magnet-tipped guidewires (FindrWIRZ); and a 12-F Lariat suture delivery device (25).

**IMPLANTATION TECHNIQUES FOR WATCHMAN AND ACP**

**PRE-PROCEDURAL IMAGING.** Baseline TEE is important to exclude pre-existing LAA thrombus and to assess for suitability for LAA closure, especially for sizing and device selection. A full 0° to 180° sweep is useful to appreciate the LAA anatomy and for accurate measurements. For WATCHMAN, the widest LAA ostium (anatomic orifice measured from the circumflex artery inferiorly to a point superiorly 1 to 2 cm within the pulmonary vein ridge) at 0°, 45°, 90°, and 135° and the available depth of the LAA (from ostium to apex of LAA) are measured. For ACP, measurements at both the short axis (30° to 60°) and the long axis (120° to 150°) of the landing zone and orifice are important. The LAA orifice represents the line from the pulmonary vein ridge to the circumflex artery (echocardiographic orifice) (Figure 5). The landing zone is measured at 10 mm within the orifice at an angle that is perpendicular to the neck axis. The LAA depth is measured from the orifice to the back wall along the neck axis. For Amulet, the landing zone is ~12 to 15 mm from the orifice due to the wider lobe.

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**FIGURE 1** WATCHMAN and 14-F Access Sheaths (Double- and Single-Curve)

There are 3 radio-opaque marker bands (33, 27, and 21 mm) on the distal sheath, which should be aligned to the left atrial appendage (LAA) "ostium" according to the selected device. PTFE = polyethylene terephthalate.
Of note, the LAA measurements are usually wider at the long axis view (corresponding to caudal projection on fluoroscopy) compared to the short axis (corresponding to the right anterior oblique [RAO] cranial).

Pre-procedural cardiac computed tomography angiography (CCTA) is also useful to examine LAA anatomy and dimension, given the superior spatial resolution and 3-dimensionality. Moreover, CCTA is good for ruling out LAA thrombi, especially when delayed imaging is acquired (negative predictive value 100%) (26). Thus, CCTA can become a noninvasive alternative to TEE in experienced CCTA centers and is increasingly routinely performed prior to LAA closures (27).

**PROCEDURAL IMAGING.** It is generally recommended that LAA closures with any current CE mark devices be performed with TEE guidance for accurate device positioning and safety, typically accompanied by general anesthesia. However, there are a few centers adept with intracardiac echocardiography (ICE) that prefer procedural ICE instead, obviating the need for general anesthesia. However, obtaining adequate LAA images can be challenging, and some overcome this problem by advancing the ICE probe into the left atrium through another transseptal puncture. There are also limited centers that rely on fluoroscopy alone (24); however, these are typically very experienced centers for LAA closure, and this is not advised for the average operator.

**VENOUS ACCESS.** Right femoral venous access is preferred because it allows more direct transseptal access than the left femoral vein does. Access site should be well prepared with the scalpel, and subcutaneous tissues separated by forceps to ease advancement of large 13- to 14-F sheaths. Manual compression, “figure-of-8” suture, or pre-closing with the 6-F Perclose ProGlide Suture-Mediated Closure System (Abbott Vascular, Temecula, California) are commonly used for hemostasis.

**TRANSSEPTAL PUNCTURE.** Transseptal puncture should be inferiorly and posteriorly located in the fossa ovalis for both WATCHMAN and ACP implantation, which is well gauged with the bicaval and short-axis TEE views, respectively. ICE is also useful to guide transseptal puncture. Very experienced operators sometimes use anatomic landmarks on fluoroscopy alone to guide punctures. Although there is a small study showing good procedural success with LAA closure through patent foramen ovale (28), it is generally advised and preferential to perform a separate transseptal puncture interpositionally that

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**TABLE 2 WATCHMAN Studies and Key Results**

<table>
<thead>
<tr>
<th>Study (Ref. #)</th>
<th>Design</th>
<th>CHADS2, Mean ± SD</th>
<th>Procedural Success, %</th>
<th>Follow-Up Duration</th>
<th>Efficacy Events</th>
<th>Important Safety Issues With WM</th>
</tr>
</thead>
<tbody>
<tr>
<td>PROTECT-AF (29,31)</td>
<td>RCT, N = 707: 2 WM; 1 warfarin</td>
<td>2.2 ± 1.2</td>
<td>90.9</td>
<td>1,065 pt-yrs (mean 1.8 yrs)</td>
<td>Primary endpoint: stroke, systemic embolism, CV death: 3.0% WM, 4.9% warfarin per 100 pt-yrs; RR: 0.62. Met noninferiority criteria.</td>
<td>Serious pericardial effusion 4.8%, procedural stroke 1.3%, device embolization 0.6%, major bleeding 3.5% (4.1% warfarin), hemorrhagic stroke 0.2% (2.5% warfarin).</td>
</tr>
<tr>
<td>PREVAIL (32)</td>
<td>RCT, N = 407: 2 WM; 1 warfarin</td>
<td>2.6 ± 1.0</td>
<td>95.1</td>
<td>18 months</td>
<td>Stroke, systemic embolism, CV, and unexplained death at 18 months: 0.064 both groups, RR: 1.07. Did not meet noninferiority criteria (90 pts at 18-month follow-up); Ischemic stroke or systemic embolism &gt;7 days met noninferiority criteria: 0.0253 WM; 0.0201 warfarin.</td>
<td>Major bleeding 4.8% (7.4% warfarin), hemorrhagic stroke 0.6% (3.7% warfarin).</td>
</tr>
<tr>
<td>CAP (30)</td>
<td>Registry, N = 460</td>
<td>2.4 ± 1.2</td>
<td>95.0</td>
<td>Median 0.4 yr</td>
<td>All-cause stroke and systemic embolism 2.3%/yr. Observed ischemic stroke rate was 77% lower than expected.</td>
<td>Procedural stroke 0%, serious pericardial effusion 2.2%.</td>
</tr>
<tr>
<td>ASAP (33)</td>
<td>Registry, N = 150</td>
<td>2.8 ± 1.2</td>
<td>94.7</td>
<td>14 months</td>
<td></td>
<td>Serious procedure- or device-related events 8.7%. Pericardial effusion with tamponade 1.3%, device embolism 1.3%, device thrombus 4.0% (with 0.7% causing stroke).</td>
</tr>
</tbody>
</table>

ASAP = ASA Plavix Feasibility Study With WATCHMAN Left Atrial Appendage Closure Technology; CAP = Continued Access Protocol; CHADS2 = congestive heart failure history, hypertension history, age ≥75 years, diabetes mellitus history, stroke or transient ischemic attack symptoms previously; CV = cardiovascular; PREVAIL = Prospective Randomized Evaluation of the WATCHMAN LAA Closure Device in Patients With Atrial Fibrillation vs. Long-Term Warfarin Therapy; PROTECT-AF = WATCHMAN Left Atrial Appendage System for Embolic Protection in Patients With Atrial Fibrillation; pt-yrs = patient-years; RCT = randomized controlled trial; RR = risk ratio; WM = WATCHMAN.
provides more direct vector orientation to access the LAA, which is more anterior and superior. Intravenous heparin is administered before or immediately following transseptal puncture to maintain an activated clotting time >250 s. It is also important to attain adequate mean left atrial pressure (~15 mm Hg) with fluid bolus for accurate measurements.

**FLUOROSCOPIC LAA MEASUREMENTS.** Following transseptal puncture, a 5-F marker pigtail is advanced into the LAA and cineangiograms are performed in multiple projections to ascertain the LAA anatomy and measurements. Caudal projections are usually better in visualizing the mid-distal LAA for the WATCHMAN device, whereas RAO cranial projections are better in visualizing ostium and proximal LAA for ACP. We typically perform ≥3 angiographic views, often aided by CCTA for angle selection. For the WATCHMAN device, we usually perform RAO (20° to 30°) caudal (20° to 30°), PA caudal (20° to 30°), and RAO (20° to 30°) cranial (10° to 20°) projections. For ACP, we usually perform RAO (30°) cranial (10°), RAO (30°) cranial (30°), and PA cranial (20° to 30°) projections.

**ACCESS SHEATH ADVANCEMENT.** A long (260-cm) J-tipped stiff 0.035-inch wire (e.g., Amplatz Super Stiff J-tip 3-mm curve) should be advanced into the left upper pulmonary vein as a rail for sheath access.
The appropriately-sized access sheath is then safely advanced to the left upper pulmonary vein ostium. To allow easier access, the venous access should be well-dilated, and the sheath gently rotated during advancement to ensure coaxial approach while crossing the interatrial septum.

For the WATCHMAN device, the 14-F access sheath is advanced deep into the LAA using a pigtail (5- to 6-F) before device introduction. RAO 20° to 30° caudal 20° to 30° angulation typically allows good visualization of the distal lobes for sheath advancement and device deployment. The access sheath is safely navigated over the pigtail into the distal segment of the LAA (Figure 2), until the corresponding radio-opaque marker band for the device size (Figure 1) is aligned with the LAA ostium. Once in position, the pigtail is removed, and often a moderate degree of catheter torque is required to maintain sheath position in the distal lobe.

For ACP, the appropriately-sized sheath/dilator is usually advanced to the left upper pulmonary vein orifice, and then the sheath is withdrawn slightly and turned counterclockwise to fall into the LAA ostium. A J-tip wire or pigtail may be used to facilitate engagement to minimize traumatizing the thin left atrium. Usually an RAO cranial projection is used for ACP sheath positioning and implantation.

**WATCHMAN SIZING AND IMPLANTATION STEPS.**

WATCHMAN sizing is based on the maximum LAA ostium diameter, which should be 17 to 31 mm to accommodate available devices. Oversizing is recommended by 9% to 25% based on the widest measurement, which generally corresponds to 2- to 4-mm oversizing. The prepped delivery system containing the compressed device is then introduced into the access sheath. The delivery system is advanced until both the distal marker bands of the delivery system and access sheath are aligned. The device is then unsheathed slowly without forward advancement of the device, preferably inducing apnea for the patient to allow stable deployment. When the device is fully unsheathed, the device position is evaluated on fluoroscopy and TEE. If it is too distal, the device may be partially recaptured and the access system withdrawn slightly, then the unsheathing process is reattempted. If the device is too proximal (or sizing or position is suboptimal), the device can be fully recaptured, and a new device and delivery system can be reattempted through the existing 14-F sheath.

Before device release, the 4 “PASS” criteria should be met: 1) position (device distal or at LAA ostium, protrusion of shoulder by <40% to 50% of device depth is acceptable); 2) anchor (testing stability by retracting the deployment knob and letting go, to assess return to original position); 3) size (device shoulder compressed 8% to 20% of original size on TEE); and 4) seal (assess TEE for any residual flow, must be <5 mm before release). When these criteria are met, the device may be released with counterclockwise rotation of the core wire for 3 to 5 turns. Final angiography and TEE assessment are then performed.

**ACP SIZING AND IMPLANTATION STEPS.**

ACP sizing depends on the widest landing zone on fluoroscopy or TEE. A standard recommendation is to upsize the device by 3 to 5 mm for ACP and 2 to 4 mm for the Amulet device from the widest measured landing zone. This degree of oversizing improves stability of the device and proper anchoring of the lobe. However, caution should be exercised if the landing zone is very elliptical to avoid dramatic oversizing (>5 mm) in the narrowest dimension.

The prepped device is advanced to the tip of the access sheath, which is positioned at the landing zone of the LAA. The first step of deployment is unsheathing by withdrawal of the delivery sheath to deploy the “ball” (Figure 5). If the position is adequate on TEE and fluoroscopy, the remainder of the lobe is then deployed. If the angle and position of the lobe at the landing zone is optimal, then the disk can be
deployed. This maneuver requires slight traction of the delivery cable during further unsheathing of the disk, to separate the lobe from the disk adequately and to ensure that the disk is deployed in the left atrium. The position and angulation of the fully unsheathed device is confirmed on TEE and fluoroscopy. If unsatisfactory at any point prior to release, the disk and lobe can be resheathed into the “ball” configuration, as long as the 2 platinum markers on the device do not enter the radio-opaque band on the sheath. If the device positioning/size is inadequate, or if the platinum markers enter beyond the radio-opaque band, then the device has to be entirely removed, and the sheath replaced.

Prior to device release, 5 signs should be present to ensure proper deployment (examples in Figure 6): 1) tire-shape of the lobe (ensuring adequate compression of the lobe and engagement of stabilizing wires); 2) separation of the lobe from the disk (ensuring good seal of disk); 3) concavity of the disk (ensuring good seal by traction of the disk from the lobe); 4) axis of the lobe (should be perpendicular to the neck axis at landing zone, to ensure proper contact of lobe walls and stabilizing wires); and 5) lobe is adequately within the circumflex artery on TEE (i.e., lobe should be deep enough such that the width of the lobe is two-thirds or more within the circumflex). If there is uncertainty about device stability, a gentle “pull” of the disk may be performed, but vigorous wiggle testing is contraindicated. Alternatively, the device can be observed for several minutes for stability prior to release. The presence of residual leak is assessed on TEE. Contrast injections can be performed through the delivery sheath to assess optimal positioning after ensuring that the system is deaired. Once a satisfactory position is achieved, the device is released with counterclockwise rotation of the delivery cable.

**Implantation Techniques for Lariat**

A pre-operative CCTA is necessary to exclude large (>40 mm) appendages and other anatomic variants (e.g., posteriorly rotated LAA under the pulmonary artery, pericardial adhesions) that preclude the use of this device, which may occur in up to 20% of cases. TEE is performed pre-procedurally to exclude LAA thrombus and during the procedure to verify the anatomic position of the EndoCATH balloon at the LAA ostium.
The procedure was well described by Bartus et al. (25) with 4 key steps: 1) pericardial and transseptal access; 2) placement of the endocardial magnet-tipped guidewire in the apex of the LAA with balloon identification of the LAA ostium; 3) connection of the epicardial and endocardial magnet-tipped guidewires; and 4) snare capture of the LAA with closure confirmation and release of the pre-tied suture for LAA ligation.

Pericardial access requires an anterior approach through the subxiphoid area with a 17-gauge epidural needle, and fluoroscopic guidance in anteroposterior and lateral views. Following epicardial access, a 0.035-inch guidewire is advanced and left in the pericardial space while the transseptal puncture is performed. The EndoCATH back-loaded with the magnet-tipped 0.025-inch endocardial guidewire is advanced to the LAA apex through the transseptal catheter. The epicardial access is then sequentially dilated to insert the 14-F guide-cannula, and the 0.035-inch epicardial magnet-tipped guidewire is then placed through the epicardial sheath and directed toward the LAA to connect with the endocardial magnet. With the EndoCATH balloon inflated at the LAA ostium, the Lariat suture is then guided to the LAA along the epicardial magnet, and looped over the LAA to snare it. The snare is closed after confirmation on TEE and left atrial angiogram, and suture tightening and cutting is then performed. A pigtail catheter is usually left in the pericardial space for several hours post-procedure.

**CLINICAL TRIALS EVALUATING SAFETY AND EFFICACY OF LAA OCCLUSION**

Several studies have evaluated the efficacy and safety of these LAA occlusion devices for stroke prevention with AF. The majority are early experience...
registries, with only 1 randomized controlled trial published to date.

**WATCHMAN.** The WATCHMAN device was studied in the multicenter PROTECT-AF (WATCHMAN Left Atrial Appendage System for Embolic Protection in Patients With Atrial Fibrillation) trial (29), where 707 patients with nonvalvular AF and CHADS2 ≥1 were randomized to the WATCHMAN device (n = 463) or to continued warfarin therapy (n = 244) in a 2:1 ratio. WATCHMAN was successfully implanted in 90.9% of cases. Warfarin was continued for 45 days with WATCHMAN and then switched to clopidogrel for 4.5 months (if there is no leak >5 mm on TEE at 45 days), with aspirin lifelong after implantation. Warfarin was discontinued in 86% of patients at 45 days and in 92% at 6 months.

The composite primary efficacy of stroke, systemic embolism, and cardiovascular death event rates met noninferiority criteria at 1,065 and 1,588 patient-years of follow-up. However, the primary adverse procedure-related events and major bleeding were higher with the WATCHMAN device (5.5% vs. 3.6% annually; risk ratio [RR]: 1.53; 95% confidence interval: 0.95 to 2.70) (Table 2) (30,31).

At 45-month (2,621 patient-years) follow-up (presented at Heart Rhythm Society 2013), the primary efficacy endpoint was significantly lower with the WATCHMAN device (2.3 events vs. 3.8 events per 100 patient-years; RR: 0.6), meeting both the noninferiority and superiority criteria. Hemorrhagic stroke (RR: 0.15), cardiovascular death (RR: 0.4), and all-cause mortality (hazard ratio: 0.66, p = 0.0379) were also significantly lower with the WATCHMAN device.

Due to early safety concerns in PROTECT-AF, the FDA mandated a second randomized trial to confirm the late PROTECT-AF and CAP registry safety results for approval of the device. Thus, the PREVAIL (Prospective Randomized Evaluation of the WATCHMAN LAA Closure Device in Patients With Atrial Fibrillation for approval of the device. Thus, the PREVAIL (PROTECT-AF and CAP registry safety results for approval of the device. Thus, the PREVAIL (PROTECT-AF and CAP registry safety results for approval of the device. Thus, the PREVAIL (PROTECT-AF and CAP registry safety results for approval of the device. Thus, the PREVAIL (PROTECT-AF and Improved safety results of PREVAIL and CAP, the FDA is anticipated to imminently approve WATCHMAN.

There was a demonstrable learning curve with improvement in technical success rate and reduction in complications with increasing experience. The implant success rate improved from 91.3% in PROTECT-AF to 95.0% in the subsequent CAP registry (p = 0.033) (which included only investigators who previously implanted WATCHMAN in PROTECT-AF), in conjunction with significant reduction in procedural time (56 min vs. 50 min, p < 0.001), there was also significant decline in procedure- or device-related safety event rates when comparing the first and second halves of PROTECT-AF and CAP, with 10.0%, 5.5%, and 3.7% of patients, respectively, experiencing events within 7 days of procedure (p = 0.006) (30).

**AMPLATZER CARDIAC PLUG.** Since the launch of the ACP in 2008, over 7,000 devices have been implanted worldwide. The ACP was evaluated in several small retrospective registries (Table 3), mostly involving single-center experiences in Europe, Canada, Asia, and Latin America (24,34-43). In aggregate, >1,100 patients were included in these registries, showing good safety profile (serious pericardial effusion ~1.7%, device embolization ~1.1%, ischemic stroke ~0.4%), and procedural success (~96.4%).

Recently, Tzikas (20) presented a pooled ACP experience of 20 European and Canadian centers inclusive of 969 patients at Transcatheter Cardiovascular Therapeutics 2013. The mean age was 74.9 years, CHA2DS2-VASc score of 4.4, and HAS-BLED (hypertension, abnormal liver function, abnormal renal function, stroke, bleeding, labile international normalized ratios, elderly [age ≥65 years], drugs, alcohol) score of 3.2. About 29% were on OAC prior to implantation. Implantation success was 97.2%, and in
93.2% of cases, the first device selected was implanted. With follow-up TEE, the closure rate (<3 mm residual flow) was 97.6%. The rate of periprocedural major adverse events (7-day death, ischemic stroke, systemic embolism, and procedure- or device-related complications requiring major cardiovascular or endovascular intervention) was 4.1% (mortality 0.6%, pericardial tamponade 1.2%, device embolization 0.2%, stroke 0.7%). The observed annual stroke rate was 2.1%, which was 63% lower than the expected 5.6% stroke rate based on CHA2DS2-VASc score, similar to other smaller registries (24,39,41).

The U.S. pivotal ACP randomized-controlled trial commenced enrollment in early 2013, randomizing AF patients with CHADS2 ≥2 to ACP versus anticoagulation (warfarin or dabigatran) in a 2:1 ratio. However, due to slow enrollment and imminent FDA approval of WATCHMAN, this study was discontinued in December 2013 after enrollment of ~80 patients. The study is being redesigned, and it is anticipated that the new randomized study will involve a non-inferiority comparison to the WATCHMAN device.

**LARIAT.** The first published single-center experience with the Lariat procedure included 89 patients in Poland (25). The mean age was 62 years, CHADS2 score was 1.9, and CHA2DS2-VASc was 2.8. Technical success was 96%. There were 2 epicardial-related complications (right ventricular puncture and superficial epigastric artery laceration) and 1 transseptal complication (hemopericardium). Major post-operative adverse events included 2 severe pericarditis, 1 late pericardial effusion, 2 unexplained sudden deaths, and 2 late strokes. Of the 65 patients undergoing TEE at 1 year, complete LAA closure was observed in 98%.

More recently, Price et al. (44) published the multicenter retrospective U.S. experience of 154 patients who underwent the Lariat procedure. The procedural time was 76.6 min and technical success was 94%, but procedural success (without procedural complication) was only 86%. Major adverse in-hospital events included: significant pericardial effusion (requiring intervention) 10.4%; bleeding requiring transfusion 4.5%; and emergent cardiac surgery 2.0%. At median 112 days follow-up, death, myocardial infarction or stroke occurred in 2.9%. TEE follow-up was performed in 63 patients revealing residual leak in 20%, and presence of thrombus in 4.8%. In summary, this study showed that even though technical success was acceptable, the Lariat procedure resulted in worrisome pericardial effusion and bleeding, thus requiring further evaluation.

## COMPLICATIONS WITH PERCUTANEOUS LAA CLOSURE AND MANAGEMENT

The acute complications with WATCHMAN and ACP appear comparable. With good technical skills and procedural planning, the risks of procedural ischemic stroke is <0.5%, serious pericardial effusion 1% to 2%, and device embolization 0.5% to 1%. Ischemic strokes may be related to procedural air embolism (inadequate device preparation or poor technique) or thrombus in LAA or on equipment. Baseline imaging to exclude pre-existing thrombus, adequate procedural anticoagulation, and meticulous and proficient techniques are important to minimize thromboembolism. Pericardial effusion causing hemodynamic compromise requires emergent pericardiocentesis, and possibly pericardial window or surgical intervention for cardiac perforation. Pericarditis related to Lariat procedures is often managed with nonsteroidal anti-inflammatories or with steroids. Device embolization is typically managed by percutaneous retrieval if feasible. A large arterial sheath through the femoral artery that is ≥2-F larger than the implanting access sheaths is often required to retrieve the embolized device, in conjunction with loop-snare and biop tome. An embolized device trapped in the left ventricle is more challenging to retrieve but can be successfully performed (Figure 7). Sometimes, surgical removal is required, especially if the device is trapped by papillary muscles or trabeculations.

Longer-term potential issues include thrombus on device and residual leak; thus, follow-up TEE or CCTA ~3 to 6 months post-procedure is typically performed (and is sometimes repeated at 1 year). Formation of thrombus on the atrial side of devices can occur in 2% to 5% of cases with the 3 devices. These occurrences are purported to occur predominantly on nonendothelialized device protrusions, such as the threaded insert with WATCHMAN and the proximal end screw with ACP, especially if implants are too deep. Thus, avoiding deep implantations creating cul-de-sacs, especially avoiding uncovered proximal LAA trabeculations, have been advised. New device designs have also been pursued to address these concerns; for example, Amulet has a recessed proximal end screw. Although there is no consensus on management, such thrombotic complications are usually managed with anticoagulation (OAC or low-molecular-weight heparin) for 8 to 12 weeks, with repeat TEE to assess for thrombus resolution before cessation of anticoagulation. Reported thromboembolic stroke event rates related to device thrombus are low: 0.3% to 0.7% (30,33).
Residual leaks occur in a fair proportion of WATCHMAN implantations, with some degree of leak seen in 32% of cases in PROTECT-AF at 12-month follow-up (36.8% >3 mm, and 63.2% ≤3 mm). However, residual leak was not associated with increased risk of subsequent thromboembolism (45), although the event rate was low and these findings were considered hypothesis generating. For ACP, leak >5 mm has not been documented; leak 3 to 5 mm occurs in 0% to 1% of cases (41), and leak <3 mm occurs in 0% to 16% of cases (35,37,39). The ACP’s low incidence of leak is presumably related to the double-disk design. Residual leak has also been demonstrated with the Lariat procedure, with variable reported incidence from 2% to 22% at follow-up TEE (25,44). In cases of residual leak >5 mm, patients may be continued on long-term anticoagulation (29); there are also case reports of performing another LAA closure with a different device for large residual leaks (46).

**SELECTION AND COMPARISON OF LEADING LAA DEVICES**

LAA device choice often depends on the availability at the institution and country. Although there is no randomized comparative study, the technical success of the leading devices (WATCHMAN and ACP) appears quite comparable, 95% to 97%. The Lariat procedure appears to have lower technical success of 93%, with even lower procedural success of 83% (due to major complications). Most operators would prefer the endocardial route and relegate epicardial approach to unsuitable anatomy for endocardial closure (e.g., large LAA with diameter >31 to 32 mm but <40 mm, or unusual anatomy such as a short neck).

Although baseline TEE is commonly done, this technology is limited by spatial resolution and often does not provide full definition of the LAA. Baseline CCTA is very useful to fully appreciate the LAA complexity, which helps with device selection and optimizes fluoroscopic views. LAA can be broadly divided into 4 different shapes (47): chicken wing, cactus, windsock, and cauliflower (Figure 5). However, LAA anatomy is highly variable and may have a combination of these characteristics. We pay particular attention to the anatomy at intended landing zones evaluating for sphericity, pectinate ridges, trabeculations, diverticula, and additional lobes. Detailed measurements are taken at the orifice, intended landing zone, and available depth (Figure 5). Using 3-dimensional CT reconstruction, we select the optimal fluoroscopic angles for the different devices: ACP/Amulet requires optimized views for the proximal/neck of LAA, whereas WATCHMAN requires better visualization of the body and distal lobes. Examples of LAA anatomy ranging from easy to challenging closures with leading devices are shown in Figures 6 and 7.

In general, both leading devices can accommodate over 95% of LAA anatomy. The LAA size is an
important consideration for selection. According to the manufacturers, the WATCHMAN device can accommodate a maximum LAA ostium between 17 mm and 31 mm, whereas ACP can accommodate a maximum LAA landing zone of 12.6 to 28.5 mm (Amulet between 12.6 mm and 32 mm). The shape of the LAA may also influence device choice. WATCHMAN is a relatively spherical device that requires as much LAA depth as the device diameter does. This may limit implantation where there is inadequate depth. There is also a threshold as to the acceptability of shoulder protrusion into the left atrium with WATCHMAN (the PET membrane covers ~50% of the proximal part of the device, and thus

**FIGURE 6** Easy to Intermediate Challenging Anatomies for LAA Closures

(A) Chicken wing LAA with moderately-angled (<90°) and gentle curve with apex of bend >15 mm from orifice, easily closed with the ACP 28-mm device (B). (C and D) Windsock LAA easily closed with the Amulet device. (E) Cactus LAA with quite eccentric landing zone being narrow in the right anterior oblique cranial projection but much wider and showing marked filamentous trabeculations in the caudal projection (F); this was moderately challenging for LAA closure with the Amulet device. (H to J) Early bifurcating bilobed LAA at ~10 mm from orifice, moderate difficulty closing with the Amulet device with lobe abutting against the carina. Abbreviations as in Figures 2 and 3.
The devices should not protrude greater than this amount. The ACP, on the other hand, only requires a depth of ~10 mm (Amulet requires depth of 12 to 15 mm). Other important shape considerations are the presence of protruding pectinate ridges, location of additional lobes and trabeculations, and angulation at the landing zones. Challenging anatologies include proximal (~10 mm from orifice) and severely sharp-angled (>90° bend) chicken wing configuration, certain cactus configuration, and limited depths. A mental visualization of how each device would optimally sit in the proximal LAA is helpful for device selection.

**CONCLUSIONS**

Percutaneous LAA closure is an emerging technology with several CE-marked devices available in many countries. The WATCHMAN device has the most
supportive data and is anticipated to be approved imminently by the FDA. For ACP, there has been a large real-world experience in the past 5 years, and a randomized trial comparing ACP with WATCHMAN is anticipated in the near future. The Lariat procedure has also gained interest lately, but early studies were concerning for high rates of serious pericardial effusion and major bleeding. There are many other devices under investigation. The current real-world experience predominantly involves patients who are not long-term anticoagulation candidates (or perceived at high risk of bleeding). This pattern of practice is expected to change if the FDA approves the WATCHMAN device for warfarin-eligible patients.

Before the pendulum swings completely in favor of LAA closure over OAC, several remaining issues should be addressed: longer-term follow-up efficacy data; comparative efficacy of LAA closure to NOAC; additive effects of OAC and LAA closure; noninferiority comparisons between different LAA devices; and updated cost-effective analyses for LAA closure.

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