The Spectrum of Devices for Percutaneous Left Atrial Appendage Occlusion

A look at current and emerging nonpharmacologic stroke prevention therapies.

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Atrial fibrillation (AF) remains the most common type of cardiac arrhythmia, with a projected prevalence of affecting more than 12 million individuals in the United States by 2050 and approximately 18 million in Europe by 2060.[1,2] AF is associated with a fivefold increase in the risk of stroke, as well as high morbidity, mortality, and health care costs.[3] Despite new therapeutic options with direct oral anticoagulants, anticoagulation is still underutilized, as one-third of AF patients at risk for stroke are not receiving oral anticoagulation in contemporary practice.[4]

It has been shown that in nonvalvular AF, thrombi typically occur in the left atrial appendage (LAA),[5] and mechanical LAA occlusion (LAAO) has emerged as an alternative therapeutic option to prevent thromboembolic events. Over the past 15 years, multiple percutaneous therapies have been developed for transcatheter LAAO, with significant improvement in periprocedural results over time.[6] This article reviews the main characteristics of and clinical results associated with the latest percutaneous LAAO devices (Table 1 and Figure 1).

ENDOCARDIAL LAAO DEVICES

Watchman and Watchman FLX Devices

The Watchman device (Boston Scientific Corporation) was the second dedicated LAAO device after the PLAATO device and is the only device to be studied in randomized trials to date.[7,8] It consists of a parachute-shaped self-expanding nitinol device with 10 active fixation barbs and a 160-mm permeable polyester (polyethylene terephthalate [PET] membrane) fabric (Figure 1A). It is available in five sizes ranging in diameter from 21 to 33 mm to accommodate LAA ostia of 17 to 31 mm. The device is delivered through a 14-F sheath and is available in three different preformed curve shapes (anterior, double, and single), although the double curve is used in most (> 90%) cases. Device size is selected according to the maximum LAA ostium diameter, and oversizing by 10% to 20% is generally recommended. The Watchman device received CE Mark approval in 2005 and US Food and Drug Administration (FDA) approval in 2015.

The Watchman FLX device (Figure 1B) is an evolution of the Watchman device with the following iterations: 10% to 20% shorter length, five different sizes (20–35 mm) for LAA ostia measuring from 15 to 32 mm, increased number of struts (18 vs 10 for the first-generation Watchman) and anchors (12 in two rows), atraumatic closed distal end to minimize risk of LAA perforation, and fully covered to minimize peridevice leaks. Despite obtaining CE Mark approval in 2015, the device was withdrawn in March 2016 due to increased device embolization rates. A new version of the Watchman FLX is being developed. An example of LAAO with the Watchman device is shown in Figure 1C and 1D.

TABLE 1. CURRENT DEVICES FOR PERCUTANEOUS LAAO

Device	Manufacturer	Design	Sizes (mm)	Sheath (F)	Approval Status
Endocardial LAAO Devices					
Watchman	Boston Scientific Corporation	Single (lobe)	21, 24, 27, 30, 33	14	CE Mark (2005); FDA (2015)
Watchman FLX			20, 24, 27, 31, 35	14	CE Mark (2015); withdrawn (2016)
Amplatzer Cardiac Plug	Abbott Vascular, formerly St. Jude Medical	Double (lobe and disc)	16, 18, 20, 22, 24, 26, 28, 30	9–13	CE Mark (2008)
Amplatzer Amulet			16, 18, 20, 22, 25, 28, 31, 34	12–14	CE Mark (2013)
WaveCrest	Biosense Webster, Inc., a Johnson & Johnson company	Single (lobe)	22, 27, 32	12	CE Mark (2013)
Occlutech	Occlutech International AB	Single (lobe)	15, 18, 21, 24, 27, 30, 33, 36, 39	12, 14	CE Mark (2016)
LAmbre	Lifetech Scientific Co., Ltd.	Double (umbrella and cover)	16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36	8–10	CE Mark (2016); CFDA (2017)
Sideris Transcatheter Patch	Custom Medical Devices	Frameless, bioabsorbable, balloon-deliverable device	15–25	13	Undergoing clinical evaluation
Ultraseal	Cardia, Inc.	Double (bulb and sail)	16, 18, 20, 22, 24, 26, 28, 30, 32	10–12	CE Mark (2016)
SeaLA	Hangzhou Valued Medtech Co., Ltd.	Double (dual disc)	16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36	9–12	Undergoing clinical evaluation
LeFort	Lepu Medical Technology (Beijing) Co., Ltd.	Single (lobe)	21–33	–	Undergoing clinical evaluation
Epicardial LAAO Devices					
Lariat	SentreHeart, Inc.	Endoepicardial	40 (W) (45 [W] Lariat +) X 20 (H) X 70 (L)	12	CE Mark (2015); FDA 510(k) (2006), surgical use only
Sierra	Aegis Medical Innovations Inc.	Epicardial	Single size	20	Undergoing clinical evaluation

Abbreviations: CFDA, China Food and Drug Administration; FDA, US Food and Drug Administration; H, height; L, length; LAAO, left atrial appendage occlusion; W, width.

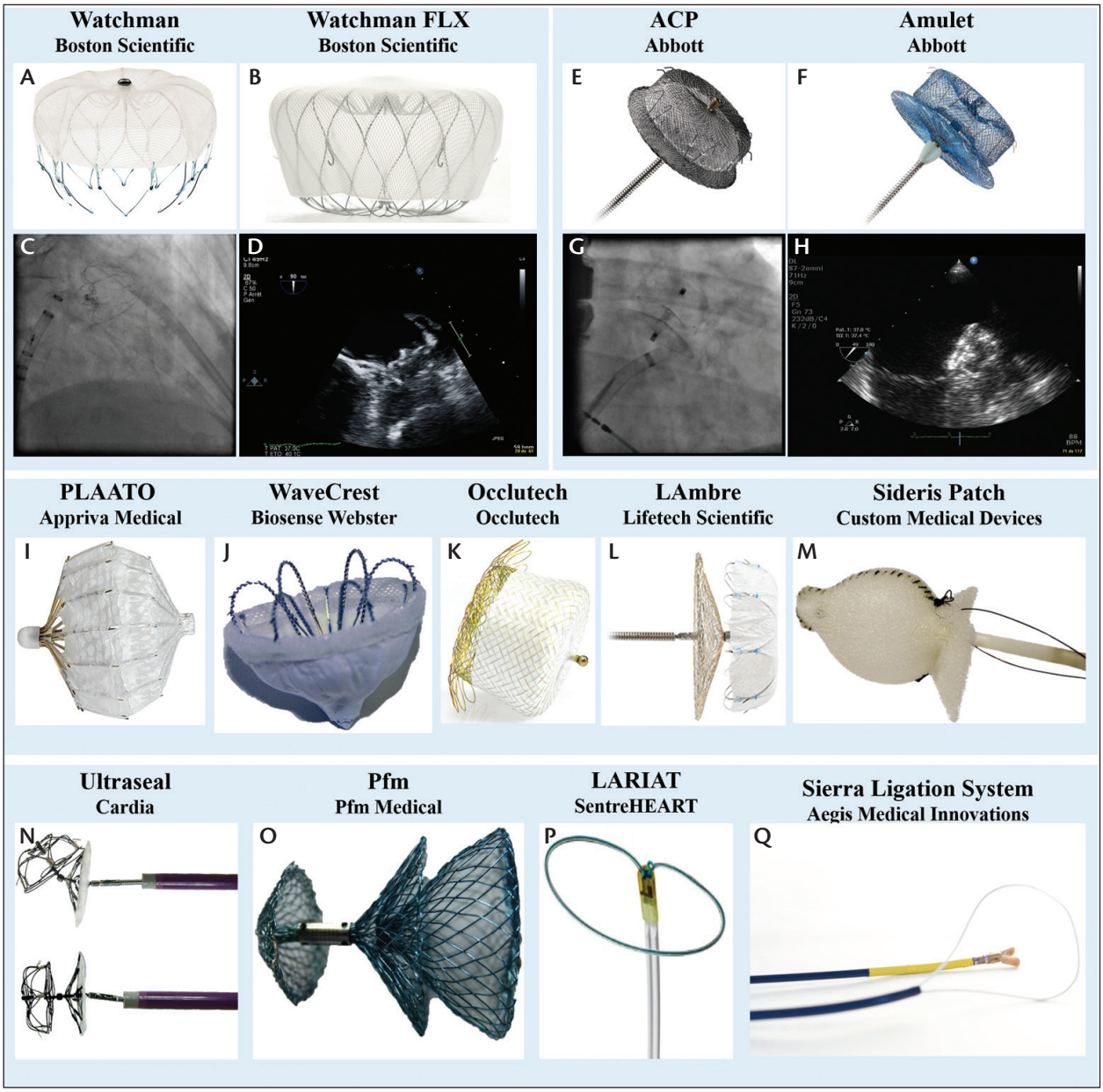

Figure 1. Percutaneous LAAO devices. The Watchman and Watchman FLX devices (A, B). Fluoroscopic and echocardiographic images of the Watchman device (C, D). ACP and Amplatzer Amulet (E, F). Fluoroscopic and echocardiographic views of the ACP device (G, H). PLAATO device (I). WaveCrest LAAO device (J). Occlutech LAA occluder (K). LAmbre LAA closure system (L). Sideris transcatheter patch (M). Ultraseal LAAO device (N). Pfm device (O). Lariat device (P). Sierra ligation system (Q). Modified with permission from Asmarats L, Rodés-Cabau J. Percutaneous left atrial appendage closure: current devices and clinical outcomes. Circ Cardiovasc Interv. 2017;10:e005359. © 2017 American Heart Association, Inc.

A recent meta-analysis of pooled, patient-level data from the PROTECT-AF (NCT00129545) and the PREVAIL trials at a mean follow-up of 47.6 ± 21.3 months and 47.9 ± 19.4 months, respectively, showed similar efficacy for the prevention of ischemic stroke and systemic embolism between LAAO and warfarin, with additional reductions in major bleeding (ie, hemorrhagic, disabling/fatal stroke) and mortality after LAAO.[9]

Amplatzer Cardiac Plug and Amplatzer Amulet Device

The Amplatzer Cardiac Plug (ACP; Abbott Vascular, formerly St. Jude Medical) is a self-expanding nitinol device with a distal lobe and a proximal disc (Figure 1E). The Amplatzer Amulet device, the second generation of the ACP, included the following modifications: the device comes preloaded in eight different sizes (14–34 mm) fitting LAA sizes from 11 to 31 mm, the proximal disc is larger (6–7 mm greater than the lobe vs 4–6 mm for ACP), and the distal lobe is longer (7.5–10 mm) with more stabilizing wires (six to 10 pairs vs six pairs for ACP) (Figure 1F). Appropriate sizing is determined by the maximum landing zone at 10 to 12 mm from the ostium, with a general oversizing of 2 to 4 mm. The Amulet device is implanted through a 12- to 14-F double-curved TorqVue 45° X 45° sheath. Further details about implantation technique can be found elsewhere.[10]

In 2016, Tzikas et al reported the largest multicenter experience with ACP (case examples shown in Figure 1G and 1H), including 1,047 patients from 22 centers, with a high 97.3% procedural success rate and 5% periprocedural adverse event rate (1.2% cardiac tamponade, 1.2% major bleeding, 0.9% stroke, 0.8% device embolization, 0.8% procedure-related death).[11] The results of an observational study, which enrolled 1,088 patients in 61 centers, were recently reported.[12] Compared with the ACP experience, successful device implantation was higher (99%) and the periprocedural adverse event rate was lower (3.2% overall, including 1.2% pericardial tamponade, 0.2% death, 0.2% stroke, 0.1% device embolization), with adequate (jet < 3 mm) LAA occlusion at 3 months in 98.2% of patients. The ongoing Amulet investigational device exemption (IDE) trial (NCT02879448) will randomize more than 1,800 patients in a 1:1 fashion to either Amulet or Watchman, with a 5-year follow-up.

The ACP and Amulet devices received CE Mark approval in 2008 and 2013, respectively. Neither device is available for commercial use in the United States.

WaveCrest LAAO System

The WaveCrest LAAO system (Biosense Webster, Inc., a Johnson & Johnson company) is a nitinol single-lobe device covered by expanded polytetrafluoroethylene, with 20 anchoring points (Figure 1J). The device is available in three different sizes (22, 27, and 32 mm), fitting LAA ostia from 14 to 32 mm, and is delivered through a 15-F sheath that allows distal contrast injection.

Reddy presented the 45-day data of the WAVECREST I trial (N = 73) at Congenital and Structural Interventions (CSI) 2013, with 92% primary efficacy for the intention-to-treat protocol and 97% for the as-treated protocol, respectively.[13] There was also a 2.7% periprocedural complication rate (two cases of cardiac tamponade). The WAVECREST postmarket clinical follow-up study (NCT03204695) will prospectively enroll 65 patients, assessing 45-day all-cause deaths, as well as device- and procedure-related events as the primary outcome.

The WaveCrest system received CE Mark approval in 2013. It is not available for commercial use in the United States.

Occlutech LAA Occluder

The Occlutech LAA occluder (Occlutech International AB) is a self-expanding, soft, cylindrically shaped nitinol mesh that is covered with a nonwoven layer (Figure 1K). The proximal section is larger to ensure good sealing, with a distal loop rim for device stability. The device is available in sizes from 18 to 33 mm and is delivered through a 12- to 14-F steerable sheath allowing 180° angulation. Oversizing of 2 to 4 mm is generally recommended.

The Occlutech device received CE Mark approval in 2016, but it was withdrawn from the market due to increased device embolization. A new version of the Occlutech LAA occluder has been developed, with improved covering nanostructure for better sealing and endothelialization and eight pairs of anchors at the midsection of the device. A clinical trial is expected to be launched in mid-2018. The device is not available for commercial use in the United States.

LAmbre LAA Closure System

The LAmbre LAA closure system (Lifetech Scientific Co., Ltd.) is a self-expanding nitinol device composed of a proximal cover—filled with sewn-in PET—and a distal umbrella with eight claws and an additional PET membrane, connected by a central waist (Figure 1L). The device is available in 15 different sizes ranging from 16 to 36 mm. Two different designs have been developed according to cover/umbrella ratio (cover 4–6 mm or 12–14 mm larger than the umbrella for standard and special devices, respectively) to suit both single- and multilobed LAA morphologies. Device sizing should generally be 4 to 8 mm larger than the LAA orifice. The device is delivered through an 8- to 10-F sheath, within 2 cm of the ostium, and then released by stepwise pushing to expose the distal umbrella, with subsequent unsheathing to release the proximal cover.

The first multicenter experience with the LAmbre device was reported by Huang et al and included 153

patients from 12 Chinese centers, with 99.4% procedural success, 3.3% periprocedural major adverse events (2% cardiac tamponade, 0.7% stroke, 0.7% major bleeding), and 99% complete LAA sealing (jet < 3 mm) at 12-month follow-up.[14]

The LAmbre LAA closure system received CE Mark approval in 2016 and is not available for commercial use in the United States.

Sideris Patch and Prolipsis

The Sideris Transcatheter Patch (Custom Medical Devices) is a frameless, bioabsorbable, balloon-deliverable device made from porous polyurethane (Figure 1M). After advancing the device through a 13-F sheath, a balloon is inflated with 3 to 10 mL of diluted contrast to diameters of 15 to 25 mm until it stretches the LAA. A surgical adhesive is applied to the distal half of the device and activated by alkaline solution injection. The supportive balloon is removed 45 minutes after adhesive activation. Initial experience included 20 patients, with 85% procedural success and one procedural complication (acute sheath thrombus).[15] Twelve additional patients have been treated with Prolipsis, the new version of the device, which enables immediate patch release with 100% full occlusion and no procedural complications.[16]

The device is not available for commercial use in either Europe or the United States.

Ultraseal

The Ultraseal LAAO device (Cardia, Inc.) is a self-expanding nitinol device with a lobe-and-disc design composed of a distal atraumatic bulb with 12 stabilizing hooks and a proximal multilayered sail made of three leaflets connected by an articulating joint that enables multidirectional movement (Figure 1N).[17] The device has been developed in nine different sizes according to bulb size (16–32 mm), and the sail is 6 mm in diameter larger than the bulb to ensure adequate sealing. The device is delivered through 10- to 12-F sheaths and may be recaptured and redeployed up to five times. Device sizing is determined by the maximum measured landing zone, with ≥ 25% oversizing.

Preliminary results of the initial multicenter experience presented by Asmarats at CSI 2017 included 80 patients, with 99% procedural success and a low 2.5% rate of periprocedural complications (one device embolization, one major bleed, and no significant pericardial effusion or in-hospital deaths), and 6% significant peridevice leaks (≥ 3 mm) at 3-month follow-up.[18]

The Ultraseal device received CE Mark in 2016 and is not available for commercial use in the United States.

SeaLA LAA Occluder

The SeaLA LAA occluder (Hangzhou Valued Medtech Co., Ltd.) is a self-expandable nitinol braiding mesh composed of a distal anchor disc (with nine anchoring hooks) and a proximal seal disc (with a plate and a waist for better sealing). The device is available in 11 different sizes and is delivered through a 9- to 12-F double-curve sheaths. The first-in-human experience with the SeaLA device was presented by Sievert at CSI 2017, including 11 successful implants in Argentina and China, with no complications.[19] A combined China Food and Drug Administration/FDA/CE Mark clinical study is planned to enroll more than 200 patients.

LeFort Device

The LeFort device (Lepu Medical Technology [Beijing] Co., Ltd.) is an umbrella-like, self-expanding nitinol device covered with permeable PET membrane and several fixation barbs, with a similar design to Watchman. The device is available in sizes ranging from 21 to 33 mm. The device is currently under clinical evaluation.

Pfm Device

The Pfm device (Pfm Medical) is a nitinol device consisting of three sections: a primary distal anchor, middle adjustable length connector, and proximal disc with secondary anchor (Figure 1O). It is delivered through a 10- to 12-F sheath. The device is currently undergoing preclinical evaluation and is not yet approved in Europe or the United States.

EPICARDIAL LAAO DEVICES

Lariat Device

The Lariat suture delivery device (SentreHeart, Inc.) allows LAA ligation by combining endocardial and epicardial approaches. After transseptal puncture, a magnetic-tipped wire is placed at the LAA apex with balloon identification of the ostium. A second magnetic wire is then advanced epicardially. Upon magnetic wire apposition, a lasso-like suture is advanced and cinched around the LAA (Figure 1P).

The largest series with the Lariat system to date included 712 patients from 18 United States centers, with a 95% success rate and a 5.3% periprocedural complication rate (3.4% significant pericardial effusion, 1.3% major bleeding, 0.5% arterial injury, 0.1% procedural death).[20]

The Lariat device received CE Mark approval in 2015 and FDA approval in 2006 for surgical soft tissue approximation but has not been approved for stroke prevention as of yet.

Sierra Ligation System

The Sierra ligation system (Aegis Medical Innovations, Inc.) allows electrocardiography-guided LAA ligation through an epicardial-only approach (Figure 1Q).[21] An appendage grasper with jaws and mounted electrodes enables identification and capture of the LAA through electrographic navigation. A hollow suture loop is then advanced over the grasper and looped around the LAA for final cinching. A feasibility study is currently ongoing in the United States and Canada (NCT02583178).

EVIDENCE GAPS

Many unanswered questions remain despite the growing body of data regarding the safety and efficacy of LAAO. First, there is a need for additional randomized clinical trials with different available devices, since Watchman remains the only device studied in randomized trials to date. However, as previously mentioned, the Amulet IDE trial will randomize patients in a 1:1 fashion to either Amulet or Watchman devices. Second, patient selection for LAAO remains controversial, and a direct comparison between LAAO and newer anticoagulants for thromboembolic prevention is lacking. The ongoing PRAGUE-17 study (NCT02426944) will randomize 400 patients with AF to either direct anticoagulation or LAAO. Finally, remaining gaps on optimal antithrombotic treatment, as well as incidence and management of device-related thrombosis following LAAO require further investigation.

CONCLUSION

In the past decade, percutaneous LAAO has been established as a valid alternative for thromboembolic prevention in nonvalvular AF patients, specifically targeting patients with contraindications to anticoagulation or at high bleeding risk. Increased operator experience and continuous iterative device innovations have resulted in improved successful implantation rates and decreased periprocedural complications. However, optimal antithrombotic treatment, randomized clinical data with different commercialized devices in anticoagulation-eligible patients, and head-to-head comparison with direct oral anticoagulants remain important caveats to be addressed in further studies. ■

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