Status of Left Atrial Appendage Closure

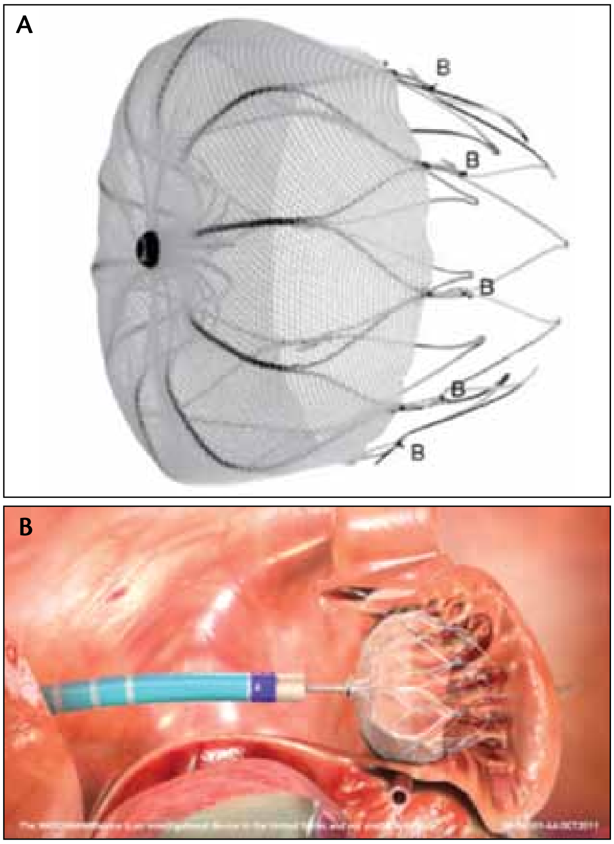
Interventional strategies developed to decrease stroke risk in patients with atrial fibrillation.

BY STEVEN J. YAKUBOV, MD, FACC, FSCAI, AND JONATHAN FORQUER, DO

Atrial fibrillation (AF) is the most common sustained cardiac dysrhythmia in the world, with more than 3 million people affected in the United States and 15 million patients worldwide. AF carries a fivefold increase in the incidence of embolic stroke and a threefold risk of mortality.[1] AF is responsible for approximately 25% of all ischemic strokes. Cardioembolic stroke as a result of AF is associated with a mortality rate of 30% at 1 year.[2,3] The lifetime risk of developing AF is one in four in those older than 40 years of age. The risk of stroke in AF increases with higher $CHADS_2$ and $CHADS_2$-VASc scores. At least 50% of patients with AF who are eligible for anticoagulation are not receiving effective anticoagul ation therapy.[4]

Oral anticoagulation is the most effective medical therapy for stroke prevention in patients with AF.[5] Unfortunately, many patients are unable to tolerate anticoagulation due to the associated risk of bleeding. In addition, discontinuation of anticoagulation is quite common, varying from 20% to 40% at 1 year.[6] Dabigatran, rivaroxaban, and apixiban are new oral anticoagulant therapies demonstrating noninferiority and/or superiority to warfarin in stroke prevention, but they also carry the risk of serious bleeding complications, as well as a higher cost.[7-9] Just as the risk of stroke and major bleeding increases with age, potential contraindications to anticoagulation also increase with age.

The left atrial appendage (LAA) has been identified by echocardiography and computed tomographic imaging as a source of thrombus development in patients with AF, with more than 90% of patients with thromboembolic events and nonvalvular AF having LAA thrombus.[10] The LAA is located between the left ventricle and the left upper pulmonary vein and usually traverses in the atrioventricular groove anteriorly and inferiorly; however, its orientation is distinctive in each individual.[11,12] LAA anatomy is variable, but it usually has an elliptical ostial segment that is free of trabeculations. The LAA is often multilobed with trabeculations in the mid and distal segments. Thrombus development in the LAA is usually a result of blood stasis due to decreased left atrial flow velocity in the AF, often accompanied by decreased left ventricle function and left atrial distention.



Images courtesy of Boston Scientific Corporation.

Figure 1. Watchman LAA closure device (Boston Scientific Corporation, Natick, MA) (A). The device is introduced through transeptal access and deployed in the LAA. Once satisfactory positioning is achieved at the ostium of LAA, the device is released, and the delivery catheter is removed (B).

Image courtesy of St. Jude Medical, Inc.

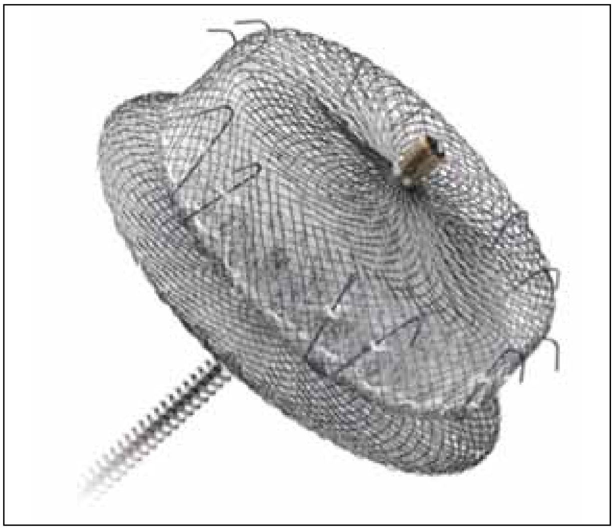


Figure 2. Amplatzer Cardiac Plug LAA closure device (St. Jude Medical, Inc., St. Paul, MN).

SURGICAL EXCLUSION OF THE LAA

Surgical exclusion of the LAA has been performed as a stand-alone procedure for anticoagulant-intolerant patients and in conjunction with surgery on the mitral or aortic valve, coronary artery bypass, or as part of the maze procedure. The results of surgical exclusion have been variable. Suture ligation has been fraught with a high propensity of late LAA patency.[13,14] Furthermore, surgical LAA has been associated with postoperative bleeding, perioperative stroke, and LAA laceration related to traction of the LAA.

PERCUTANEOUS LAA CLOSURE DEVICES

The first transseptal device developed for LAA closure was studied in PLAATO (Percutaneous Left Atrial Appendage Transcatheter Occlusion Study).[15] The device was a self-expanding nitinol cage with a polytetrafluoroethylene membrane, anchoring in the LAA via hooks on the struts of the cage. PLAATO demonstrated the feasibility of LAA exclusion in patients with nonvalvular AF and an inability to tolerate anticoagulation.[14] Although the annualized ischemic stroke rate was favorable compared to expected rates predicted by $CHADS_2$ scoring (3.8% vs 6.6%), complications related to the procedure hampered adoption of the device.

Watchman Device

The Watchman device is a self-expanding nitinol frame with fixation barbs and a polyester membrane covering of the cage (Figure 1A). It comes in various sizes (21–33 mm) and is deployed after measurement of the LAA ostium by transesophageal echocardiography (TEE). Transseptal puncture is usually performed at a posterior and inferior location of the septum to ensure adequate introduction of the delivery sheath into the body of the LAA. The delivery catheter is placed over a pigtail catheter in the LAA. The Watchman device is deployed by gentle retraction of the delivery sheath, and the device is placed at the ostium of the LAA. TEE and angiography are used to assess the adequacy of final deployment prior to release (Figure 1B). The Watchman device has been assessed in the PROTECT-AF CAP registry, ASAP, and the PREVAIL trials. More than 2,200 implantations have been performed worldwide to date.[16-18]

PROTECT-AF evaluated the Watchman device versus warfarin in 707 patients with nonvalvular AF and a $CHADS_2$ score > 1. Anticoagulation after device placement was continued for 40 days followed by aspirin and clopidogrel for 6 months and then aspirin alone indefinitely. The composite endpoint of stroke, cardiovascular death, and systemic embolization was 3% versus 4.9% in the control group at 18 months (relative risk reduction of 38%).

Cardiovascular death, overall mortality, and hemorrhagic stroke all favored patients receiving the Watchman device. However, ischemic stroke, mainly due to periprocedural air embolism, was higher in the Watchman group (2.2% vs 1.6%). Safety endpoints were also less favorable with the Watchman device, with 10.6% of patients developing serious procedural complications; pericardial effusions occurred in 4.8%. Although there were no device-related deaths, device embolization and the need for surgical intervention occurred in 2.2% of patients.

The CAP registry evaluated 460 patients, showing a significant decrease in procedure-related complications with greater operator experience. This registry showed a

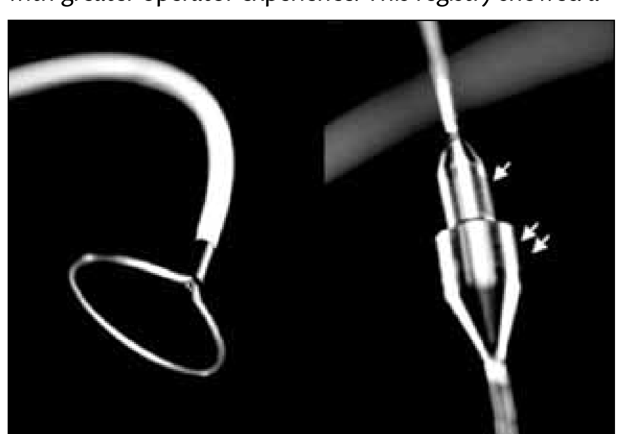


Image courtesy of SentreHeart, Inc.

Figure 3. The Lariat closure device (SentreHeart, Inc., Redwood City, CA).

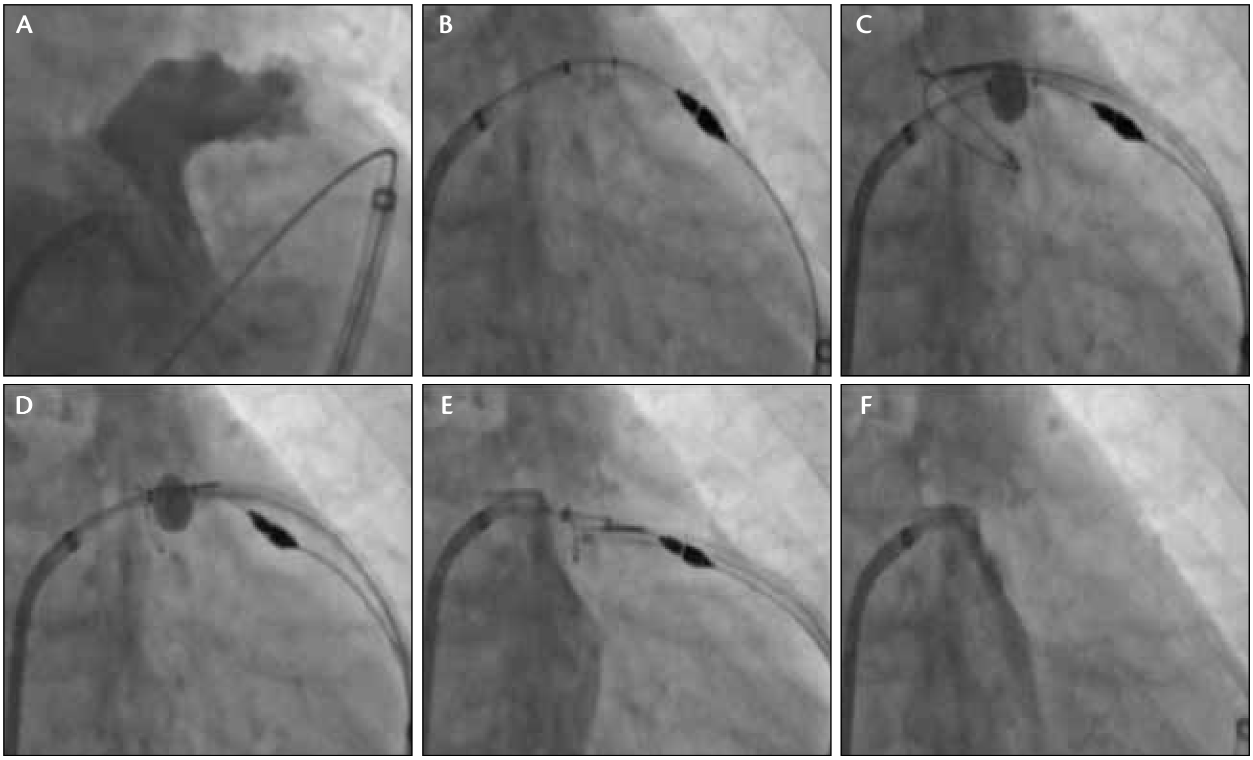


Figure 4. All images are in the right anterior oblique projection. Left atrial angiography identifies the ostium and body of the LAA (A). Attachment of the magnet-tipped endocardial and epicardial guidewires (B) allows for the Lariat suture delivery device to be guided over the LAA by the magnet-tipped epicardial guidewire, using an over-the-wire approach (C). After verification of the correct position of the snare with the balloon catheter (D), left atrial angiography is performed prior to the release of the pretied suture to exclude the existence of a remnant trabeculated LAA lobe (E). Final left atrial angiography is performed to verify LAA exclusion (F). Reprinted from the Journal of the American College of Cardiology, in press, Bartus K, Han FT, Bednarek J, et al, Percutaneous left atrial appendage suture ligation using the Lariat device in patients with atrial fibrillation: initial clinical experience., Copyright (2012), with permission from Elsevier.[20]

significant decline in serious periprocedural events (7.7% vs 3.7%) and pericardial effusion (5% vs 2.2%).

The ASAP study evaluated closure of the LAA with the Watchman device in patients ineligible for oral anticoagulation. There was a 77% risk reduction in ischemic stroke in patients treated with the Watchman device.

The PREVAIL study is a prospective, randomized clinical trial of 407 high-risk patients with atrial fibrillation randomized to the Watchman device or warfarin. Enrollment is complete and awaiting 6-month follow-up.

Amplatzer Cardiac Plug

The Amplatzer cardiac plug (ACP) is a self-expanding nitinol frame consisting of a lobe and disc, which has many features of the devices used for percutaneous closure of atrial septal defects (Figure 2). The ACP is delivered after sheath introduction into the LAA. Transseptal puncture in an inferior and posterior location enhances success of proper device deployment. The distal lobe of the device is deployed by retracting the sheath. After satisfactory positioning of the lobe, the flat disc, which is larger than the LAA ostium, is deployed, covering the opening of the LAA. Successful implantation is defined by proper appearance (compression) of the lobe, separation of the lobe and disc on angiography, concave shape of the disc, at least two-thirds of the lobe located distal in the LAA to the circumflex artery on echocardiography, and correct angulation of the lobe and disc in relation to the plane of the LAA ostium. Device size selection is made by measuring the landing zone of the device lobe (approximately 1 cm from the plane of the LAA ostium) by TEE and angiography. Slight device oversizing is encouraged for complete LAA occlusion and proper lobe appearance.

More than 4,000 patients worldwide have undergone implantation of these devices in the LAA. The initial European experience showed successful occlusion of the LAA in 96% of patients and a serious complication rate of 7%, including ischemic stroke, device embolization, and pericardial effusion.[19] In the United States, only a feasibility trial has been completed to date, and an upcoming pivotal clinical trial is planned to begin soon.

Lariat Device

Percutaneous closure of the LAA via a combined transseptal and pericardial approach consists of the following equipment: 0.025- and 0.035-inch magnet-tipped guidewires (FindrWirz, SentreHeart, Inc.), a 15-mm compliant balloon catheter (EndoCath, SentreHeart, Inc.), and a 12-F suture delivery device (Lariat) (Figure 3). Preprocedural computed tomographic angiography is very helpful in planning the procedure to assess the size and shape of the LAA for positioning the FinderWirz guidewires and to plan a pericardial access approach. Percutaneous pericardial access is achieved first from a midline approach using a 17-gauge pericardial needle. The direction of access is toward the left shoulder of the patient, with the access site on the anterior surface of the heart. Tenting of the pericardium prior to puncture is seen using small amounts of contrast injection through the needle. Verification of pericardial access is seen with the characteristic appearance of a small amount of contrast in the pericardial space and proper placement of a 0.035-inch guidewire in the pericardial space. A 14-F, soft-tipped epicardial sheath is then placed.

An inferior and posterior position is desirable for transseptal access, using an 8.5-F SL1 transseptal catheter (St. Jude Medical, Inc.). Left atriagram is performed in a right anterior oblique caudal projection to visualize the LAA body and lobes. The 0.025-inch endocardial wire is advanced through the balloon catheter to the apex of the LAA. The balloon catheter is placed at the ostium of the LAA for identification of the proper landing zone of closure and for support during Lariat placement. The 0.035-inch epicardial wire is placed through the epicardial sheath, creating a magnetic union with the endocardial wire. The Lariat is then advanced over the epicardial wire and closed at the site of the LAA opening. Once satisfactory closure is confirmed by TEE and angiography, the endocardial wire and balloon are removed, and final tightening of the suture is performed. The Lariat is removed, and the suture is cut near the LAA ostium. A pericardial drain is left in place overnight (Figure 4).

In the single-center PLACE-2 registry, 85 of 89 patients had successful LAA ligation, with 81 patients having complete closure immediately.[20] Three patients had a small residual leak (< 2 mm), and one had a leak > 3 mm. There was one pericardial access-related complication and two transseptal access-related complications. Other complications included pericarditis, late pericardial effusion, and two late unexplained sudden deaths from nonembolic strokes. At follow-up, 95% of patients had complete closure by TEE at 6 months (77 of 81) and 98% closure at 1 year (63 of 65). Therefore, the Lariat device has demonstrated highly effective rates of LAA closure with limited complications.

Figure 5. The Wavecrest LAA closure device (Coherex Medical, Inc., Salt Lake City, UT).

Coherex Wavecrest LAA Occluder

The Coherex Wavecrest LAA occluder device is a nitinol-based device with a mesh covering of the LAA ostium (Figure 5). After feasibility of this device has been established with excellent clinical results, a CE Mark clinical trial will recruit patients in Europe. There is a planned pivotal trial in the United States in 2013.

FUTURE CONSIDERATIONS

As evidence accumulates regarding the benefit of LAA closure in reducing the incidence of cardioembolic stroke in patients with AF, there are other frontiers of investigation to pursue. The use of closure devices in conjunction with AF ablation may enhance ablation success because nearly 25% of AF recurrence is near the LAA ostium. Devices that may interrupt those AF signals, such as the Lariat, may be helpful. The impact of intracardiac LAA occluders may play a role in this also. New techniques to enhance device placement, such as better guiding catheters, safer ways to access the pericardial space, and enhanced imaging, are being developed. Finally, improvements and innovation of all devices will make these procedures less complicated with decreased procedural times and enhanced safety. ■

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1. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation: a major contributor to stroke in the elderly. Arch Intern Med. 1987;147:1561-1564.
2. Kannel WB, Benjamin EJ. Status of the epidemiology of atrial fibrillation. Med Clin North Am. 2008;92:17-40.
3. Lloyd-Jones D, Adams R, Carnethon M, et al. Heart disease and stroke statistics—2009 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation. 2009;119:e21-181.
4. Hart RG, Halperin JL. Atrial fibrillation and stroke: concepts and controversies. Stroke. 2001;32:803-808.
5. Hart RG, Pearce LA, Aguilar MI. Meta-analysis: antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation. Ann Intern Med. 2007;146:857-867.
6. Connolly SJ, Ezekowitz MD, Yusuf S, et al. Dabigatran versus warfarin in patients with atrial fibrillation. N Engl J Med. 2009;361:1139-1151.
7. Granger CB, Alexander JH, McMurray JJ, et al. Apixaban versus warfarin in patients with atrial fibrillation. N Engl J Med. 2011;365:981-992.
8. Patel MR, Mahaffey KW, Garg J, et al; ROCKET AF Investigators. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. N Engl J Med. 2011;365:883-891.
9. Wallentin L, Yusuf S, Ezekowitz MD, et al; RE-LY Investigators. Efficacy and safety of dabigatran compared with warfarin at different levels of international normalised ratio control for stroke prevention in atrial fibrillation: an analysis of the RE-LY trial. Lancet. 2010;376:975-983.
10. Thambidorai SK, Murray RD, Parakh K, et al. Utility of transesophageal echocardiography in identification of thrombogenic milieu in patients with atrial fibrillation (an ACUTE ancillary study). Am J Cardiol. 2005;96:935-941.
11. Kerut EK. Anatomy of the left atrial appendage. Echocardiography. 2008;25:669-673.
12. Su P, McCarthy KP, Ho SY. Occluding the left atrial appendage: anatomical considerations. Heart. 2008;94:1166-1170.
13. Donnino R, Tunick PA, Kronzon I. Left atrial appendage thrombus outside of a "successful" ligation. Eur J Echocardiogr. 2008;9:397-398.
14. Healy JS, Crystal E, Lamy A, et al. Left Atrial Appendage Occlusion Study (LAAOS): results of a randomized controlled pilot study of left atrial appendage occlusion during bypass surgery in patients at risk for stroke. Am Heart J. 2005;150:288-293.
15. Ostermayer SH, Reisman M, Kramer PH, et al. Percutaneous Left Atrial Appendage Transcatheter Occlusion (PLAATO system) to prevent stroke in high-risk patients with non-rheumatic atrial fibrillation: results from the international multi-center feasibility trials. J Am Coll Cardiol. 2005;46:9-14.
16. Sick PB, Schuler G, Hauptmann KE, et al. Initial worldwide experience with the Watchman left atrial appendage system for stroke prevention in atrial fibrillation. J Am Coll Cardiol. 2007;49:1490-1495.
17. Holmes DR, Reddy VY, Turi ZG, et al. Percutaneous closure of the left atrial appendage versus warfarin therapy for prevention of stroke in patients with atrial fibrillation: a randomised noninferiority trial. Lancet. 2009;374:534-542.
18. Reddy VY, Holmes D, Doshi SK, et al. Safety of percutaneous left atrial appendage closure: results from the Watchman Left Atrial Appendage System for Embolic Protection in Patients with AF (PROTECT AF) clinical trial and the Continued Access Registry. Circulation. 2011;123:417-424.
19. Park JW, Bethencourt A, Sievert H, et al. Left atrial appendage closure with Amplatzer Cardiac Plug in atrial fibrillation—initial European experience. Catheter Cardiovasc Interv. 2011;77:700-706.
20. Bartus K, Han FT, Bednarek J, et al. Percutaneous left atrial appendage suture ligation using the Lariat device in patients with atrial fibrillation: initial clinical experience. J Am Coll Cardiol. In press.