

Medical Policy



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Title: **Percutaneous Left-Atrial Appendage Closure Devices for Stroke Prevention in Atrial Fibrillation**

Professional

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DESCRIPTION

Stroke prevention in atrial fibrillation is an important consideration. Treatment with anticoagulant medications is the most common approach to stroke prevention. The majority of embolic strokes originate from the left atrial appendage; therefore, left atrial appendage occlusion devices offer a non-pharmacologic alternative to anticoagulant medications.

Stroke is the most serious complication of atrial fibrillation. The estimated incidence of stroke in non-treated patients with atrial fibrillation is 5% per year. Stroke associated with atrial fibrillation is primarily embolic in nature, tends to be more severe than the typical ischemic stroke, and causes higher rates of mortality and disability. As a result, stroke prevention is one of the main goals of atrial fibrillation treatment.

Stroke occurs primarily as a result of thromboembolism from the left atrium. The lack of atrial contractions in atrial fibrillation leads to blood stasis in the left atrium, and this low flow state increases the risk for thrombosis. The area of the left atrium with the lowest blood flow in atrial fibrillation, and, therefore, the highest risk of thrombosis, is the left-atrial appendage (LAA). It has been estimated that 90% of left-atrial thrombi occur in the LAA.

The main treatment for stroke prevention in atrial fibrillation is anticoagulation, which has proven efficacy. Warfarin is the predominant agent in clinical use. A number of newer anticoagulant medications have recently received U.S. Food and Drug Administration (FDA) approval for this indication and have demonstrated noninferiority to warfarin in clinical trials. While anticoagulation is effective for stroke prevention, there is an increased risk of bleeding. Also, warfarin requires frequent monitoring and adjustments, as well as lifestyle changes. Dabigatran does not require monitoring. However, unlike warfarin, the antithrombotic effects of dabigatran are not reversible with any currently available hemostatic drugs.

Surgical removal, or exclusion, of the LAA is often performed in patients with atrial fibrillation who are undergoing open heart surgery for other reasons. Percutaneous LAA closure devices have been developed as a nonpharmacologic alternative to anticoagulation for stroke prevention in atrial fibrillation. The devices may prevent stroke by occluding the LAA, thus preventing thrombus formation.

Several versions of LAA occlusion devices have been developed. The WATCHMAN® left atrial appendage system (Boston Scientific, Maple Grove, MN) is a self-expanding nickel titanium device. It has a polyester covering and fixation barbs for attachment to the endocardium. Implantation is performed percutaneously through a catheter delivery system, utilizing venous access and transseptal puncture to enter the left atrium. Following implantation, patients are anticoagulated with warfarin or alternate agents for approximately 1-2 months. After this period, patients are maintained on antiplatelet agents (i.e., aspirin and/or clopidogrel) indefinitely. The Lariat® Loop Applicator is a suture delivery device that is intended to close a variety of surgical wounds in addition to left atrial appendage closure. The Cardioblate® closure device developed by Medtronic Corp. is currently being tested in clinical studies. The Amplatzer® cardiac plug (St. Jude Medical, Minneapolis, MN), is FDA-approved for closure of atrial septal defects but has not received FDA approval for LAA closure device. The Percutaneous LAA Transcatheter Occlusion (PLAATO) device (eV3, Plymouth, MN) has also been evaluated in research studies but has not received FDA approval.

Regulatory Status

There are currently no percutaneous LAA closure devices with FDA approval. The WATCHMAN® device was considered for FDA approval in 2009 based on the results of the Percutaneous Closure of the Left Atrial Appendage Versus Warfarin Therapy for Prevention of Stroke in Patients with Atrial Fibrillation (PROTECT-AF) randomized controlled trial. While the FDA advisory panel for this topic voted in favor of approval, the FDA did not grant final approval after concluding that further studies of efficacy and safety were necessary.

At least two other devices, referred to earlier, have been studied for left atrial appendage occlusion, but are not approved in the U.S. for percutaneous closure of the left atrial appendage. The Lariat® Loop Applicator device (SentreHEART, Inc, Redwood City, CA) is a suture delivery

system that received 510(k) marketing clearance from the FDA in 2006. The intended use is to facilitate suture placement and knot tying in surgical applications where soft tissues are being approximated or ligated with a pre-tied polyester suture. The Amplatzer Amulet® device (St. Jude Medical, Plymouth, MN) has a CE approval in Europe for left atrial appendage closure, but is not currently approved in the U.S. for any indication.

POLICY

The use of percutaneous left-atrial appendage closure devices for the prevention of stroke in atrial fibrillation is considered **experimental / investigational**.

RATIONALE

The evidence on the efficacy of left-atrial appendage (LAA) closure devices consists of numerous case series of various occlusion devices, and one randomized controlled trial (RCT) of the Watchman device that compared LAA closure to warfarin anticoagulation. Evidence on each different device will be reviewed separately, since the devices are not similar in design and each may have its own unique considerations.

Watchman device

The single RCT published is the PROTECT-AF study, (1) which was a randomized, unblinded trial that evaluated the noninferiority of an LAA closure device compared to warfarin for stroke prevention in atrial fibrillation. The trial randomized 707 patients from 59 centers in the U.S. and Europe to the WATCHMAN® device or warfarin treatment in a 2:1 ratio. Mean follow-up was 18 +/- 10 months. The primary efficacy outcome was a composite endpoint of stroke (ischemic or hemorrhagic), cardiovascular or unexplained death, or systemic embolism. There was also a primary safety outcome, which was a composite endpoint of excessive bleeding (intracranial or gastrointestinal [GI] bleeding) and procedure-related complications (pericardial effusion, device embolization, or procedure-related stroke).

The primary efficacy outcome occurred at a rate of 3.0 per 100 patient-years in the LAA closure group compared to 4.9 per 100 patient-years in the warfarin group (rate ratio [RR]: 0.62; 95% credible interval [CrI]: 0.35-1.25). Based on these outcomes, the probability of noninferiority was greater than 99.9%. For the individual components of the primary outcome, cardiovascular/unexplained death and hemorrhagic stroke were higher in the warfarin group. In contrast, ischemic stroke was higher in the LAA closure group at 2.2 per 100 patient-years compared to 1.6 per 100 patient-years in the warfarin group (RR: 1.34; 95% CrI: 0.60-4.29).

The primary safety outcome occurred more commonly in the LAA closure group, at a rate of 7.4 per 100 patient-years compared to 4.4 per 100 patient-years in the warfarin group (RR: 1.69; 95% CrI: 1.01-3.19). The excess in adverse event rates for the LAA closure group were primarily the result of early adverse events associated with placement of the device. The most frequent type of complication related to LAA closure device placement was pericardial effusion requiring intervention, which occurred in 4.8% of patients (22/463).

Longer term follow-up from the PROTECT AF study was reported by Reddy et al. in 2012. (2) At a mean follow-up of 2.3 years, the results were similar to the initial report. The relative risk for the composite primary outcome in the Watchman group compared to anticoagulation was 0.71, and this met non-inferiority criteria with a confidence of >99%. Complications were more common in the Watchman group, with an estimated rate of 5.6%/year in the Watchman group compared to 3.6%/year in the warfarin group.

In addition to this RCT, a number of case series have reported on outcomes on the Watchman device. The published case series are primarily small and intended to establish safety and feasibility of the device. (3-8) A larger case series of 143 patients from Europe was published in 2011. (6) This series reported that successful implantation was achieved in 96% (137/143) of patients and that serious complications occurred in 7.0% (10/143). Complications included stroke (n=3), device embolization (n=2), and pericardial effusion (n=5). Another larger series was reported by Reddy et al., (7) primarily focusing on the adverse event rate from a registry of 460 patients who received the WATCHMAN® device. Serious pericardial effusion occurred in 2.2% of patients, and there were no deaths or periprocedural strokes reported. Bayard et al. (3) reported on 180 patients with nonrheumatic atrial fibrillation and a contraindication to warfarin and who were treated with the Percutaneous Left Atrial Appendage Transcatheter Occlusion (PLAATO) device. Placement was successful in 90% of patients. Two patients died within 24 hours of the procedure (1.1%), and 6 patients had cardiac tamponade (3.3%), with 2 requiring surgical drainage. During a follow-up of 129 patient-years, there were 3 strokes, for a rate of 2.3% per year. Other case reports and small case series report complications, including multiple reports of thrombus formation at the site of device placement. (9-11)

Lariat® device

The available evidence on the efficacy of the Lariat device consists of a number of small case series. The largest case series was reported by Bartus et al. in 2012. (12) This study enrolled 89 patients with atrial fibrillation and either a contraindication to warfarin or previous warfarin failure. A total of 85/89 (96%) had successful left atrial ligation, and 81/89 (91%) had complete closure immediately. There were 3 access-related complications, 2 cases of severe pericarditis postoperatively, 1 late pericardial effusion, and 2 cases of unexplained sudden death. There were 2 late strokes, which the authors did not attribute to an embolic source. At one year of follow-up, complete closure was documented by echocardiography in 98% of available patients (n=65). In a smaller, earlier series from the same research group, (13) 13 patients were treated with the Lariat device, 11 of whom were treated as part of percutaneous radiofrequency ablation for atrial fibrillation. One of the 11 procedures was terminated due to unsuccessful placement, and the other 10 procedures were successful, with complete closure verified on echocardiography. There was one procedural complication in which the snare was unable to be removed and needed to be retrieved by thoracoscopy.

Massumi et al. (14) reported on 21 patients with atrial fibrillation and contraindications to anticoagulation. A total of 20/21 patients had successful atrial closure, which was documented by echocardiography to be intact at a mean follow-up of 96 days. No patients had a stroke during a mean follow-up of approximately one year. There were complications reported in 5/21 patients. One patient had right ventricular perforation and tamponade requiring surgical intervention. One patient developed pleuro-pericarditis that required multiple drainage procedures. Three additional patients developed pericarditis within 30 days of the procedure.

Amplatzer® Cardiac Plug device

The available evidence on use of the Amplatzer device for left atrial occlusion consists of a number of case series. The largest series identified was by Nietlispach et al., (15) which included 152 patients from a single institution in Europe. Short-term complications occurred in 9.8% (15/152). Longer-term adverse outcomes occurred in 7% of patients, including 2 strokes, 1 peripheral embolization, and 4 episodes of major bleeding. Device embolization occurred in 4.6% (7/152) of patients.

Other smaller series of patients treated with the Amplatzer device include a series of 86 patients from Portugal, (16) 37 patients from Italy, (17) 35 patients from Spain, (18) 21 patients from Poland, (19) and 20 patients from China. (20) All of these series reported high procedural success, but also reported various complications such as vascular complications, air embolism, esophageal injury, cardiac tamponade, and device embolization.

Ongoing clinical trials

There are currently a number of additional ongoing clinical trials of LAA closure devices. (21) Of studies listed online at ClinicalTrials.gov, there are at least 4 randomized, controlled trials listed:

- NCT01182441. (Evaluation of the Watchman® LAA Closure Device in Patients with Atrial Fibrillation Versus Long-term Warfarin Therapy [PREVAIL trial]). This is a study of LAA closure versus warfarin using the WATCHMAN® device. Eligibility for PREVAIL includes a CHADS score (a clinical risk prediction score of atrial-fibrillation-related stroke) of 2 or greater, or a CHADS score of 1 with other indicators of high risk, indicating a patient population with a higher risk of stroke compared to the PROTECT-AF trial. This trial plans to enroll 475 patients with an estimated completion date of November 2015. Other nonrandomized, single-group studies are in progress evaluating the safety and efficacy of various LAA closure devices.
- NCT01628068. ELIGIBLE (Efficacy of Left atrial Appendage Closure After GastroIntestinal Bleeding) study. This is a study of 120 patients with a history of GI bleed randomized to left atrial occlusion or usual care with anticoagulation. Expected completion date is July 2014.
- NCT01363895. Interventional Strategies in Treatment of Atrial Fibrillation: Percutaneous Closure of the Left Atrial Appendage Versus Catheter Ablation. This is a study that randomizes 120 patients with atrial fibrillation to left atrial closure with the Watchman device or catheter ablation. Estimated completion date is November 2013.
- NCT01118299. AMPLATZER Cardiac Plug Clinical Trial. This trial randomizes 3,000 patients with atrial fibrillation to left atrial occlusion with the Amplatzer® cardiac plug versus optimal medical care. Estimated completion date is June 2017.

Summary

LAA occlusion devices are nonpharmacologic alternatives to anticoagulation for patients with atrial fibrillation. Currently, there are no devices that have FDA-approval for this indication in the U.S., but at least 3 different devices (Watchman®, Lariat®, and Amplatzer®) have been evaluated for this purpose. Case series have demonstrated that these devices can be successfully implanted percutaneously in most patients. Complications such as pericardial effusion and tamponade are

reported in available studies at a rate of 2-5%. Periprocedural stroke has been reported uncommonly. One randomized, controlled trial compared the WATCHMAN® device to warfarin and reported noninferiority on a composite outcome of stroke, cardiovascular/unexplained death, or systemic embolism after 2 years of follow-up. There were a higher number of complications in the LAA closure group, primarily due to early complications associated with the device placement. Longer term outcomes past 2 years have not been reported. For the Lariat and Amplatzer devices, there were no controlled trials identified. Case series of these devices report high procedural success but also numerous complications.

Given the lack of FDA approval, the limited data regarding impact on net health outcome from controlled trials, and the potential for complications, left atrial appendage closure devices are considered investigational.

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

CPT/HCPCS

0281T Percutaneous transcatheter closure of the left atrial appendage with implant, including fluoroscopy, transseptal puncture, catheter placement(s), left atrial appendage angiography, radiological supervision and interpretation

DIAGNOSES

Experimental / Investigational on all diagnoses related to this medical policy.

REVISIONS

12-20-2013 Policy added to the bcbks.com web site.

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