Medical Coverage Policy | Percutaneous Left Atrial Appendage Closure Devices for Stroke Prevention in Atrial Fibrillation

EFFECTIVE DATE: 10|01|2023
POLICY LAST REVIEWED: 08|21|2024

OVERVIEW

Stroke prevention in patients with atrial fibrillation (AF) is an important goal of treatment. Treatment with anticoagulant medications is the most common approach to stroke prevention. Because most embolic strokes originate from the left atrial appendage, occlusion of the left atrial appendage may offer a nonpharmacologic alternative to anticoagulant medications to lower the risk of stroke. Multiple percutaneously deployed devices are being investigated for left atrial appendage closure (LAAC). Two types of left atrial appendage devices (the Watchman and Amplatzer Amulet devices) have approval from the U.S. Food and Drug Administration (FDA) for stroke prevention in patients with AF.

This policy is applicable to Commercial Products only. For Medicare Advantage Plans, see Related Policies section.

MEDICAL CRITERIA

Commercial Products

The use of a device with U.S. Food and Drug Administration (FDA) approval for percutaneous left atrial appendage closure (e.g., the Watchman or Amplatzer Amulet) may be considered medically necessary for the prevention of stroke in individuals with atrial fibrillation when the following criteria is met:

- There is an increased risk of stroke and systemic embolism based on CHADS2 score or CHA2DS2-VASc score, and;
- Systemic anticoagulation therapy is recommended, and;
- The long-term risks of systemic anticoagulation outweigh the risks of the device implantation

PRIOR AUTHORIZATION

Commercial Products

Prior authorization is recommended and obtained via the online tool for participating providers. See Related Policies section.

POLICY STATEMENT

Commercial Products

Percutaneous left atrial appendage closure is considered medically necessary when the criteria above is met.

The use of other percutaneous left atrial appendage closure devices, including but not limited to the Lariat and Amplatzer Cardiac Plug devices, for stroke prevention in individuals with atrial fibrillation is considered not medically necessary because these devices do not have FDA approval for left arterial appendage (LAA) closure. In addition, the evidence is insufficient to determine the effects of the technology on health outcomes.

For Medicare Advantage Plans, see Related Policies section.

COVERAGE

Benefits may vary between groups and contracts. Please refer to the appropriate Benefit Booklet, Evidence of Coverage or Subscriber Agreement for applicable surgery benefits/coverage.

BACKGROUND

Atrial fibrillation (AF) is the most common type of irregular heartbeat, affecting at least 2.7 million people in the U.S. Risk of AF has been found to be lower in Black, Hispanic and Asian patients relative to White patients, including following adjustment for demographic and AF risk factors.3,4, Stroke is the most serious complication of AF. The estimated incidence of stroke in nontreated patients with AF is 5% per year; despite a lower risk of AF, Black and Hispanic patients have an increased risk of stroke compared with White patients. Stroke associated with AF is primarily embolic, tends to be more severe than the typical ischemic stroke, and causes higher rates of mortality and disability. As a result, stroke prevention is a main goal of AF treatment.

Stroke in AF occurs primarily as a result of thromboembolism from the left atrium. The lack of atrial contractions in AF 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 AF, 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 AF is anticoagulation, which has proven efficacy. The risk for stroke among patients with AF is evaluated using several factors. Two commonly used scores, the CHADS2 score and the CHA2DS2-VASc score are described below in Table 1. Warfarin is the predominant agent in clinical use. A number of newer anticoagulant medications, including dabigatran, rivaroxaban apixaban, and edoxaban have received U.S. Food and Drug Administration (FDA) approval for stroke prevention in nonvalvular AF and have demonstrated noninferiority to warfarin in clinical trials. While anticoagulation is effective for stroke prevention, it carries an increased risk of bleeding. Also, warfarin requires frequent monitoring and adjustments as well as lifestyle changes. Newer agents do not require the frequent monitoring seen with warfarin therapy; however, specific reversal agents do not exist for all of these agents. The 2018 American College of Chest Physicians guidelines (updated from 2012) recommend that CHA2DS2VASc be used to evaluate stroke risk, and patients initially identified as having a low stroke risk should not be given antithrombotic therapy. In addition, they recommend bleeding risk assessments be given to every patient at every patient contact and that "potentially modifiable bleeding risk factors" should be the initial focus.

Table 1. $CHADS_2$ and $CHADS_2$-VASc Scores to Predict Ischemic Stroke Risk in Patients With Atrial Fibrillation

Letter	Clinical Characteristics	Points Awarded
C	Congestive heart failure (signs/symptoms of heart failure confirmed with objective evidence of cardiac dysfunction)	1
H	Hypertension (resting blood pressure >140/90 mmHg on at least 2 occasions or current antihypertensive pharmacologic treatment)	1
A	Age ≥75 y	2
D	Diabetes (fasting glucose >125 mg/dL or treatment with oral hypoglycemic agent and/or insulin)	1
S	Stroke or transient ischemic attack (includes any history of cerebral ischemia)	2
V	Vascular disease (prior myocardial infarction, peripheral arterial disease, or aortic plaque)	1
A	Age 65-74 y	1
Sc	Sex category of female (female sex confers higher risk)	1

Adapted from Lip et al (2018) and January et al (2014).

Bleeding is the primary risk associated with systemic anticoagulation. Risk scores have been developed to estimate the risk of significant bleeding in patients treated with systemic anticoagulation, such as the HAS-BLED score, which has been validated to assess the annual risk of significant bleeding in patients with AF treated with warfarin. The score ranges from 0 to 9, based on clinical characteristics, including the presence of hypertension, renal and liver function, history of stroke, bleeding, labile international normalized ratios, age, and drug/alcohol use. Scores of 3 or greater are considered to be associated with a high risk of bleeding, potentially signaling the need for closer monitoring of patients for adverse risks, closer monitoring of international normalized ratios, or differential dose selections of oral anticoagulants or aspirin.

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

Several versions of LAA occlusion devices have been developed. The PLAATO system (ev3 Endovascular) was the first device to be approved by the FDA for LAA occlusion. The device was discontinued in 2007 for commercial reasons, and intellectual property was sold to manufacturers of the Watchman system. The Watchman Left Atrial Appendage System (Boston Scientific) 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, using venous access and transseptal puncture to enter the left atrium. Transesophageal echocardiography and fluoroscopy are used to guide the procedure. Following implantation, patients receive anticoagulation with warfarin or alternative agents for approximately 1 to 2 months. After this period, patients are maintained on antiplatelet agents (ie, aspirin and/or clopidogrel) indefinitely. The Watchman FLX device is a next-generation Watchman device that is also FDA-approved for LAAC. This device is based on the design of the Watchman device, is fully recapturable and repositionable, and was made to occlude a wider size range of LAA than the original Watchman device. The Amplatzer cardiac plug (St. Jude Medical), is FDA-approved for closure of atrial septal defects but not for LAAC. A second-generation device developed for the specific indication of LAAC, the Amplatzer Amulet (Abbott), received FDA approval in August 2021. The Amplatzer Amulet consists of a nitinol mesh disc to seal the ostium of the LAA and a nitinol mesh distal lobe, to be positioned within the LAA. The device is preloaded within a delivery sheath. The Percutaneous LAA Transcatheter Occlusion device (ev3) has also been evaluated in research studies but has not received FDA approval. The Occlutech ™ (Occlutech) Left Atrial Appendage Occluder has received a CE mark for coverage in Europe. The Cardioblate ™ closure device (Medtronic) is currently being tested in clinical studies.

The Lariat Loop Applicator is a suture delivery device approved by the FDA, intended to close a variety of surgical wounds. It is not specifically approved for LAAC. While the Watchman and other devices are implanted in the endocardium, the Lariat is a non-implant epicardial device.

In September 2021, the FDA sent a letter to healthcare providers indicating that women undergoing percutaneous LAA closure may be at higher risk of adverse procedural outcomes than men. This was based on an analysis of registry data from 49,357 patients who underwent LAA closure with the Watchman device. When adjusted for multiple confounding factors, the study found women were more likely than men to experience any adverse event, major adverse events, and major bleeding. Women also had a significantly higher risk of death (adjusted odds ratio [OR], 2.01; 95% confidence interval [CI] 1.31 to 3.09) but absolute risk was low for both women and men (0.3% vs. 0.1%). In their letter, the FDA stated that they believe the benefits continue to outweigh the risks for approved LAA closure devices when used in accordance with their instructions for use.

The optimal study design for evaluating the efficacy of percutaneous LAAC for the prevention of stroke in AF is a randomized controlled trial (RCT) that includes clinically relevant measures of health outcomes. The rate of ischemic stroke during follow-up is the primary outcome of interest, along with rates of systemic embolization, cardiac events, bleeding complications, and death. For the LAAC devices, the appropriate comparison group could be oral anticoagulation, no therapy (for patients who have a prohibitive risk for oral anticoagulation), or open surgical repair.

Ideally, percutaneous LAAC devices would represent an alternative to oral anticoagulation for the prevention of stroke in patients with AF However, during the post implantation period the LAAC device may be associated with increased thrombogenicity, therefore, anticoagulation is used during the periprocedural period. Most studies evaluating percutaneous LAAC devices have included patients who are eligible for anticoagulation.

In 2002, the PLAATO system (ev3 Endovascular) was the first device to be approved by the FDA for LAA occlusion. The device was discontinued in 2007 for commercial reasons, and intellectual property was sold to manufacturers of the Watchman system.

In 2015, the Watchman™ Left Atrial Appendage Closure Technology (Boston Scientific) was approved by the FDA through the premarket approval process by the Left Atrial Appendage Versus Warfarin Therapy for

Prevention of Stroke in Patients with Atrial Fibrillation randomized controlled trial. In 2020, the Watchman FLX device (Boston Scientific) was approved by the FDA based on the single-arm, nonrandomized PINNACLE FLX study. The Amplatzer™ Amulet™ Left Atrial Appendage Occluder (Abbott) received FDA approval in 2021 through the premarket approval process based on results from the Amplatzer Amulet Left Atrial Appendage Occluder Randomized Controlled Trial (Amulet IDE Trial). The Watchman and Amplatzer Amulet devices are indicated to reduce the risk of thromboembolism from the LAA in patients with nonvalvular AF who:

- Are at increased risk for stroke and systemic embolism based on CHADS2 or CHA2DS2-VASc scores and are recommended for anticoagulation therapy;
- Are deemed by their physicians to be suitable for anticoagulation therapy; and
- Have an appropriate rationale to seek a nonpharmacologic alternative to anticoagulation therapy, taking into account the safety and effectiveness of the device compared to anticoagulation therapy.

Several other devices are being evaluated for LAA occlusion but are not approved in the U.S. for percutaneous LAAC. In 2006, the Lariat ™ Loop Applicator device (SentreHEART), a suture delivery system, was cleared for marketing by the FDA through the 510(k) process. The intended use is to facilitate suture placement and knot tying in surgical applications where soft tissues are being approximated or ligated with a pretied polyester suture. The Amplatzer Cardiac Plug device (St. Jude Medical) and WaveCrest™ (Johnson & Johnson Biosense Webster) have CE approval in Europe for LAAC but are not currently approved in the U.S. for this indication.

For individuals who have AF who are at increased risk for embolic stroke who receive an FDA-approved percutaneous LAAC device (e.g., the Watchman or Amulet device), the evidence includes RCTs and observational studies. Relevant outcomes are overall survival, morbid events, and treatment-related morbidity. The most relevant evidence for the Watchman device comes from 2 industry-sponsored RCTs comparing the Watchman device with anticoagulation alone. One trial reported noninferiority on a composite outcome of stroke, cardiovascular/unexplained death, or systemic embolism after 2 years of follow-up, with continued benefits with the Watchman device after 4 years of follow-up. The second trial did not demonstrate noninferiority for the same composite outcome but did demonstrate noninferiority of the Watchman device to warfarin for late ischemic stroke and systemic embolization. Patient-level meta-analyses at 5-year follow-up for the 2 Watchman trials reported that the Watchman device is noninferior to warfarin on the composite outcome of stroke, systemic embolism, and cardiovascular death. Also, the Watchman was associated with lower rates of major bleeding, particularly hemorrhagic stroke, and mortality over the long term. Evidence for the Amplatzer Amulet device comes from 2 RCTs comparing the Amulet and Watchman devices, one of which was a short-term trial that assessed periprocedural outcomes at 45 days. The second trial comparing the Amulet and Watchman devices found the Amulet device to be noninferior to the Watchman device after 18 months of follow-up for a composite efficacy outcome that included ischemic stroke or systemic embolism and for a composite safety outcome that included all-cause mortality, major bleeding or procedure-related complications. One additional RCT evaluated the use of either the Amplatzer Amulet or Watchman device versus anticoagulants; subgroup analyses according to device were not performed. After up to 4 years of follow-up, the study found LAAC with either the Watchman or Amulet was noninferior to anticoagulants for a composite outcome that included stroke, transient ischemic attack (TIA), systemic embolism, clinically significant bleeding, significant periprocedural or device-related complications, or cardiovascular mortality. Among patients in which the long-term risk of systemic anticoagulation exceeds the procedural risk of device implantation, the net health outcome will be improved. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have AF who are at increased risk for embolic stroke who receive a percutaneous LAAC device other than the Watchman device or Amplatzer Amulet device (eg, Lariat or Amplatzer Cardiac Plug), the evidence includes several nonrandomized comparator studies and uncontrolled observational studies. Relevant outcomes are overall survival, morbid events, and treatment-related morbidity. One nonrandomized study that compared outcomes among patients undergoing LAAC with the Lariat device with patients receiving anticoagulant or antiplatelet therapy reported fewer thromboembolic events in the group receiving the Lariat device. Evidence from other observational studies of these devices which report high procedural

success but also numerous complications. In addition, these devices do not have U.S. FDA approval for LAAC. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

CODING

Commercial Products

The following code(s) is medically necessary when the criteria above has been met:

33340 Percutaneous transcatheter closure of the left atrial appendage with endocardial implant, including fluoroscopy, transseptal puncture, catheter placement(s), left atrial angiography, left atrial appendage angiography, when performed, and radiological supervision and interpretation

RELATED POLICIES

Medicare Advantage Plans National and Local Coverage Determinations
Prior Authorization via Web-Based Tool for Procedures

PUBLISHED

Provider Update, October 2024
Provider Update, August 2023
Provider Update, October 2022
Provider Update, September 2021
Provider Update, December 2020

REFERENCES

1. Center for Medicare & Medicaid Services. National Coverage Determination (NCD) for Percutaneous Left Atrial Appendage Closure (LAAC) (20.34). 2016; https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=367&ncdver=1&NCAId=281&bc=AAAAAAAACAAAAA%3d%3d&. Accessed March 21, 2024.
2. Mou L, Norby FL, Chen LY, et al. Lifetime Risk of Atrial Fibrillation by Race and Socioeconomic Status: ARIC Study (Atherosclerosis Risk in Communities). Circ Arrhythm Electrophysiol. Jul 2018; 11(7): e006350. PMID 30002066
3. Dewland TA, Olgin JE, Vittinghoff E, et al. Incident atrial fibrillation among Asians, Hispanics, blacks, and whites. Circulation. Dec 03 2013; 128(23): 2470-7. PMID 24103419
4. Gardener H, Sacco RL, Rundek T, et al. Race and Ethnic Disparities in Stroke Incidence in the Northern Manhattan Study. Stroke. Apr 2020; 51(4): 1064-1069. PMID 32078475
5. Guo J, Gabriel N, Magnani JW, et al. Racial and Urban-Rural Difference in the Frequency of Ischemic Stroke as Initial Manifestation of Atrial Fibrillation. Front Public Health. 2021; 9: 780185. PMID 34805085
6. Lip GYH, Banerjee A, Boriani G, et al. Antithrombotic Therapy for Atrial Fibrillation: CHEST Guideline and Expert Panel Report. Chest. Nov 2018; 154(5): 1121-1201. PMID 30144419
7. January CT, Wann LS, Alpert JS, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol. Dec 02 2014; 64(21): e1-76. PMID 24685669
8. Lip GY, Frison L, Halperin JL, et al. Comparative validation of a novel risk score for predicting bleeding risk in anticoagulated patients with atrial fibrillation: the HAS-BLED (Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile INR, Elderly, Drugs/Alcohol Concomitantly) score. J Am Coll Cardiol. Jan 11 2011; 57(2): 173-80. PMID 21111555
9. Food and Drug Administration. Summary of Safety and Effectiveness Data. WATCHMAN Left Atrial Appendage Closure Device with Delivery System and WATCHMAN FLX Left Atrial Appendage Closure Device with Delivery System. https://www.accessdata.fda.gov/cdrh_docs/pdf13/P130013S035B.pdf. Accessed March 18, 2024.
10. Food and Drug Administration. Approval Letter: Amplatzer Amulet Left Atrial Appendage Occluder; 2021. https://www.accessdata.fda.gov/cdrh_docs/pdf20/P200049A.pdf. Accessed March 21, 2024.
11. Food and Drug Administration. Left Atrial Appendage Occlusion (LAAO) Devices Potentially Associated with Procedural Outcome Differences Between Women and Men: Letter to Health Care

Providers. https://public4.pagefreezer.com/browse/FDA/28-09-2021T17:30/https://www.fda.gov/medical-devices/letters-health-care-providers/left-atrial-appendage-occlusion-laao-devices-potentially-associated-procedural-outcome-differences. Accessed March 19, 2024.
12. Darden D, Duong T, Du C, et al. Sex Differences in Procedural Outcomes Among Patients Undergoing Left Atrial Appendage Occlusion: Insights From the NCDR LAAO Registry. JAMA Cardiol. Nov 01 2021; 6(11): 1275-1284. PMID 34379072
13. Food and Drug Administration. Approval Letter: WATCHMAN LAA Closure Technology. 2015; http://www.accessdata.fda.gov/cdrh_docs/pdf13/p130013a.pdf. Accessed March 20, 2024.
14. Reddy VY, Doshi SK, Kar S, et al. 5-Year Outcomes After Left Atrial Appendage Closure: From the PREVAIL and PROTECT AF Trials. J Am Coll Cardiol. Dec 19 2017; 70(24): 2964-2975. PMID 29103847
15. Bode WD, Patel N, Gehi AK. Left atrial appendage occlusion for prevention of stroke in nonvalvular atrial fibrillation: a meta-analysis. J Interv Card Electrophysiol. Jun 2015; 43(1): 79-89. PMID 25711953
16. Briceno DF, Villablanca P, Cyrille N, et al. Left Atrial Appendage Occlusion Device and Novel Oral Anticoagulants Versus Warfarin for Stroke Prevention in Nonvalvular Atrial Fibrillation: Systematic Review and Meta-Analysis of Randomized Controlled Trials. Circ Arrhythm Electrophysiol. Oct 2015; 8(5): 1057-64. PMID 26226997
17. Holmes DR, Doshi SK, Kar S, et al. Left Atrial Appendage Closure as an Alternative to Warfarin for Stroke Prevention in Atrial Fibrillation: A Patient-Level Meta-Analysis. J Am Coll Cardiol. Jun 23 2015; 65(24): 2614-2623. PMID 26088300
18. Li X, Wen SN, Li SN, et al. Over 1-year efficacy and safety of left atrial appendage occlusion versus novel oral anticoagulants for stroke prevention in atrial fibrillation: A systematic review and meta-analysis of randomized controlled trials and observational studies. Heart Rhythm. Jun 2016; 13(6): 1203-14. PMID 26724488
19. Lip GY, Lane DA. Stroke prevention in atrial fibrillation: a systematic review. JAMA. May 19 2015; 313(19): 1950-62. PMID 25988464
20. Price MJ, Reddy VY, Valderrabano M, et al. Bleeding Outcomes After Left Atrial Appendage Closure Compared With Long-Term Warfarin: A Pooled, Patient-Level Analysis of the WATCHMAN Randomized Trial Experience. JACC Cardiovasc Interv. Dec 28 2015; 8(15): 1925-1932. PMID 26627989
21. Noelck N, Papak J, Freeman M, et al. Effectiveness of Left Atrial Appendage Exclusion Procedures to Reduce the Risk of Stroke: A Systematic Review of the Evidence. Circ Cardiovasc Qual Outcomes. Jul 2016; 9(4): 395-405. PMID 27407055
22. Sahay S, Nombela-Franco L, Rodes-Cabau J, et al. Efficacy and safety of left atrial appendage closure versus medical treatment in atrial fibrillation: a network meta-analysis from randomised trials. Heart. Jan 15 2017; 103(2): 139-147. PMID 27587437
23. Wei Z, Zhang X, Wu H, et al. A meta-analysis for efficacy and safety evaluation of transcatheter left atrial appendage occlusion in patients with nonvalvular atrial fibrillation. Medicine (Baltimore). Aug 2016; 95(31): e4382. PMID 27495048
24. Tereshchenko LG, Henrikson CA, Cigarroa J, et al. Comparative Effectiveness of Interventions for Stroke Prevention in Atrial Fibrillation: A Network Meta-Analysis. J Am Heart Assoc. May 20 2016; 5(5). PMID 27207998
25. Bajaj NS, Kalra R, Patel N, et al. Comparison of Approaches for Stroke Prophylaxis in Patients with Non-Valvular Atrial Fibrillation: Network Meta-Analyses of Randomized Controlled Trials. PLoS One. 2016; 11(10): e0163608. PMID 27706224
26. Hanif H, Belley-Cote EP, Alotaibi A, et al. Left atrial appendage occlusion for stroke prevention in patients with atrial fibrillation: a systematic review and network meta-analysis of randomized controlled trials. J Cardiovasc Surg (Torino). Feb 2018; 59(1): 128-139. PMID 28215062
27. 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 non-inferiority trial. Lancet. Aug 15 2009; 374(9689): 534-42. PMID 19683639
28. Reddy VY, Doshi SK, Sievert H, et al. Percutaneous left atrial appendage closure for stroke prophylaxis in patients with atrial fibrillation: 2.3-Year Follow-up of the PROTECT AF (Watchman Left Atrial

Appendage System for Embolic Protection in Patients with Atrial Fibrillation) Trial. Circulation. Feb 12 2013; 127(6): 720-9. PMID 23325525
29. Reddy VY, Sievert H, Halperin J, et al. Percutaneous left atrial appendage closure vs warfarin for atrial fibrillation: a randomized clinical trial. JAMA. Nov 19 2014; 312(19): 1988-98. PMID 25399274
30. Alli O, Doshi S, Kar S, et al. Quality of life assessment in the randomized PROTECT AF (Percutaneous Closure of the Left Atrial Appendage Versus Warfarin Therapy for Prevention of Stroke in Patients With Atrial Fibrillation) trial of patients at risk for stroke with nonvalvular atrial fibrillation. J Am Coll Cardiol. Apr 30 2013; 61(17): 1790-8. PMID 23500276
31. Holmes DR, Kar S, Price MJ, et al. Prospective randomized evaluation of the Watchman Left Atrial Appendage Closure device in patients with atrial fibrillation versus long-term warfarin therapy: the PREVAIL trial. J Am Coll Cardiol. Jul 08 2014; 64(1): 1-12. PMID 24998121
32. Osmancik P, Herman D, Neuzil P, et al. Left Atrial Appendage Closure Versus Direct Oral Anticoagulants in High-Risk Patients With Atrial Fibrillation. J Am Coll Cardiol. Jun 30 2020; 75(25): 3122-3135. PMID 32586585
33. Osmancik P, Herman D, Neuzil P, et al. 4-Year Outcomes After Left Atrial Appendage Closure Versus Nonwarfarin Oral Anticoagulation for Atrial Fibrillation. J Am Coll Cardiol. Jan 04 2022; 79(1): 1-14. PMID 34748929
34. Lam YY, Yip GW, Yu CM, et al. Left atrial appendage closure with AMPLATZER cardiac plug for stroke prevention in atrial fibrillation: initial Asia-Pacific experience. Catheter Cardiovasc Interv. Apr 01 2012; 79(5): 794-800. PMID 21542102
35. Montenegro MJ, Quintella EF, Damonte A, et al. Percutaneous occlusion of left atrial appendage with the Amplatzer Cardiac PlugTM in atrial fibrillation. Arq Bras Cardiol. Feb 2012; 98(2): 143-50. PMID 22286325
36. 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. Apr 01 2011; 77(5): 700-6. PMID 20824765
37. 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. Feb 01 2011; 123(4): 417-24. PMID 21242484
38. Swaans MJ, Post MC, Rensing BJ, et al. Percutaneous left atrial appendage closure for stroke prevention in atrial fibrillation. Neth Heart J. Apr 2012; 20(4): 161-6. PMID 22231152
39. Reddy VY, Möbius-Winkler S, Miller MA, et al. Left atrial appendage closure with the Watchman device in patients with a contraindication for oral anticoagulation: the ASAP study (ASA Plavix Feasibility Study With Watchman Left Atrial Appendage Closure Technology). J Am Coll Cardiol. Jun 25 2013; 61(25): 2551-6. PMID 23583249
40. Boersma LV, Schmidt B, Betts TR, et al. Implant success and safety of left atrial appendage closure with the WATCHMAN device: peri-procedural outcomes from the EWOLUTION registry. Eur Heart J. Aug 2016; 37(31): 2465-74. PMID 26822918
41. Dukkipati SR, Kar S, Holmes DR, et al. Device-Related Thrombus After Left Atrial Appendage Closure: Incidence, Predictors, and Outcomes. Circulation. Aug 28 2018; 138(9): 874-885. PMID 29752398
42. Jazayeri MA, Vuddanda V, Turagam MK, et al. Safety profiles of percutaneous left atrial appendage closure devices: An analysis of the Food and Drug Administration Manufacturer and User Facility Device Experience (MAUDE) database from 2009 to 2016. J Cardiovasc Electrophysiol. Jan 2018; 29(1): 5-13. PMID 28988455

43. Lakkireddy D, Thaler D, Ellis CR, et al. Amplatzer Amulet Left Atrial Appendage Occluder Versus Watchman Device for Stroke Prophylaxis (Amulet IDE): A Randomized, Controlled Trial. Circulation. Nov 09 2021; 144(19): 1543-1552. PMID 34459659
44. Galea R, De Marco F, Meneveau N, et al. Amulet or Watchman Device for Percutaneous Left Atrial Appendage Closure: Primary Results of the SWISS-APERO Randomized Clinical Trial. Circulation. Mar 08 2022; 145(10): 724-738. PMID 34747186
45. Galea R, Meneveau N, De Marco F, et al. One-Year Outcomes After Amulet or Watchman Device for Percutaneous Left Atrial Appendage Closure: A Prespecified Analysis of the SWISS-APERO Randomized Clinical Trial. Circulation. Feb 06 2024; 149(6): 484-486. PMID 37875064
46. Lakkireddy D, Thaler D, Ellis CR, et al. 3-Year Outcomes From the Amplatzer Amulet Left Atrial Appendage Occluder Randomized Controlled Trial (Amulet IDE). JACC Cardiovasc Interv. Aug 14 2023; 16(15): 1902-1913. PMID 37587599
47. Landmesser U, Schmidt B, Nielsen-Kudsk JE, et al. Left atrial appendage occlusion with the AMPLATZER Amulet device: periprocedural and early clinical/echocardiographic data from a global prospective observational study. EuroIntervention. Sep 20 2017; 13(7): 867-876. PMID 28649053
48. Landmesser U, Tondo C, Camm J, et al. Left atrial appendage occlusion with the AMPLATZER Amulet device: one-year follow-up from the prospective global Amulet observational registry. EuroIntervention. Aug 03 2018; 14(5): e590-e597. PMID 29806820
49. Hildick-Smith D, Landmesser U, Camm AJ, et al. Left atrial appendage occlusion with the Amplatzer™ Amulet™ device: full results of the prospective global observational study. Eur Heart J. Aug 07 2020; 41(30): 2894-2901. PMID 32243499
50. Nielsen-Kudsk JE, Korsholm K, Damgaard D, et al. Clinical Outcomes Associated With Left Atrial Appendage Occlusion Versus Direct Oral Anticoagulation in Atrial Fibrillation. JACC Cardiovasc Interv. Jan 11 2021; 14(1): 69-78. PMID 33413867
51. Chatterjee S, Herrmann HC, Wilensky RL, et al. Safety and Procedural Success of Left Atrial Appendage Exclusion With the Lariat Device: A Systematic Review of Published Reports and Analytic Review of the FDA MAUDE Database. JAMA Intern Med. Jul 2015; 175(7): 1104-9. PMID 25938303
52. Price MJ, Gibson DN, Yakubov SJ, et al. Early safety and efficacy of percutaneous left atrial appendage suture ligation: results from the U.S. transcatheter LAA ligation consortium. J Am Coll Cardiol. Aug 12 2014; 64(6): 565-72. PMID 25104525
53. 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. Jul 09 2013; 62(2): 108-118. PMID 23062528
54. Massumi A, Chelu MG, Nazeri A, et al. Initial experience with a novel percutaneous left atrial appendage exclusion device in patients with atrial fibrillation, increased stroke risk, and contraindications to anticoagulation. Am J Cardiol. Mar 15 2013; 111(6): 869-73. PMID 23312129
55. Miller MA, Gangireddy SR, Doshi SK, et al. Multicenter study on acute and long-term safety and efficacy of percutaneous left atrial appendage closure using an epicardial suture snaring device. Heart Rhythm. Nov 2014; 11(11): 1853-9. PMID 25068574
56. Gafoor S, Franke J, Bertog S, et al. Left atrial appendage occlusion in octogenarians: short-term and 1-year follow-up. Catheter Cardiovasc Interv. Apr 01 2014; 83(5): 805-10. PMID 24259397
57. Lakkireddy D, Afzal MR, Lee RJ, et al. Short and long-term outcomes of percutaneous left atrial appendage suture ligation: Results from a US multicenter evaluation. Heart Rhythm. May 2016; 13(5): 1030-1036. PMID 26872554
58. Bartus K, Bednarek J, Myc J, et al. Feasibility of closed-chest ligation of the left atrial appendage in humans. Heart Rhythm. Feb 2011; 8(2): 188-93. PMID 21050893

59. Stone D, Byrne T, Pershad A. Early results with the LARIAT device for left atrial appendage exclusion in patients with atrial fibrillation at high risk for stroke and anticoagulation. Catheter Cardiovasc Interv. Jul 2015; 86(1): 121-7. PMID 23765504
60. Fink T, Schlüter M, Tilz RR, et al. Acute and long-term outcomes of epicardial left atrial appendage ligation with the second-generation LARIAT device: a high-volume electrophysiology center experience. Clin Res Cardiol. Dec 2018; 107(12): 1139-1147. PMID 29881879
61. Dar T, Afzal MR, Yarlagadda B, et al. Mechanical function of the left atrium is improved with epicardial ligation of the left atrial appendage: Insights from the LAFIT-LARIAT Registry. Heart Rhythm. Jul 2018; 15(7): 955-959. PMID 29477973
62. Litwinowicz R, Bartus M, Burysz M, et al. Long term outcomes after left atrial appendage closure with the LARIAT device-Stroke risk reduction over five years follow-up. PLoS One. 2018; 13(12): e0208710. PMID 30566961
63. Litwinowicz R, Bartus M, Malec-Litwinowicz M, et al. Left Atrial Appendage Occlusion for Secondary Stroke Prevention in Patients with Atrial Fibrillation: Long-Term Results. Cerebrovasc Dis. 2019; 47(3-4): 188-195. PMID 31121584
64. Litwinowicz R, Bartus M, Kapelak B, et al. Reduction in risk of stroke and bleeding after left atrial appendage closure with LARIAT device in patients with increased risk of stroke and bleeding: Long term results. Catheter Cardiovasc Interv. Nov 15 2019; 94(6): 837-842. PMID 30884101
65. Nietlispach F, Gloekler S, Krause R, et al. Amplatzer left atrial appendage occlusion: single center 10-year experience. Catheter Cardiovasc Interv. Aug 01 2013; 82(2): 283-9. PMID 23412815
66. Kefer J, Vermeersch P, Budts W, et al. Transcatheter left atrial appendage closure for stroke prevention in atrial fibrillation with Amplatzer cardiac plug: the Belgian Registry. Acta Cardiol. Dec 2013; 68(6): 551-8. PMID 24579432
67. Guérios EE, Schmid M, Gloekler S, et al. Left atrial appendage closure with the Amplatzer cardiac plug in patients with atrial fibrillation. Arq Bras Cardiol. Jun 2012; 98(6): 528-36. PMID 22584492
68. Danna P, Proietti R, Sagone A, et al. Does left atrial appendage closure with a cardiac plug system reduce the stroke risk in nonvalvular atrial fibrillation patients? A single-center case series. Pacing Clin Electrophysiol. Mar 2013; 36(3): 347-53. PMID 23252940
69. Lopez-Minguez JR, Eldoayen-Gragera J, Gonzalez-Fernandez R, et al. Immediate and one-year results in 35 consecutive patients after closure of left atrial appendage with the Amplatzer Cardiac Plug. Rev Esp Cardiol. Feb 2013;66(2):90-97. PMID 22939161
70. Streb W, Szymała M, Kukulski T, et al. Percutaneous closure of the left atrial appendage using the Amplatzer Cardiac Plug in patients with atrial fibrillation: evaluation of safety and feasibility. Kardiol Pol. 2013; 71(1): 8-16. PMID 23348528
71. Cruz-González I, González-Ferreiro R, Freixa X, et al. Left atrial appendage occlusion for stroke despite oral anticoagulation (resistant stroke). Results from the Amplatzer Cardiac Plug registry. Rev Esp Cardiol (Engl Ed). Jan 2020; 73(1): 28-34. PMID 31036510
72. Santoro G, Meucci F, Stolcova M, et al. Percutaneous left atrial appendage occlusion in patients with non-valvular atrial fibrillation: implantation and up to four years follow-up of the AMPLATZER Cardiac Plug. EuroIntervention. Feb 2016; 11(10): 1188-94. PMID 25354761
73. Meerkin D, Butnaru A, Dratva D, et al. Early safety of the Amplatzer Cardiac Plug™ for left atrial appendage occlusion. Int J Cardiol. Oct 09 2013; 168(4): 3920-5. PMID 23890886
74. Wiebe J, Bertog S, Franke J, et al. Safety of percutaneous left atrial appendage closure with the Amplatzer cardiac plug in patients with atrial fibrillation and contraindications to anticoagulation. Catheter Cardiovasc Interv. Apr 01 2014; 83(5): 796-802. PMID 24327462

75. Urena M, Rodés-Cabau J, Freixa X, et al. Percutaneous left atrial appendage closure with the AMPLATZER cardiac plug device in patients with nonvalvular atrial fibrillation and contraindications to anticoagulation therapy. J Am Coll Cardiol. Jul 09 2013; 62(2): 96-102. PMID 23665098
76. Gloekler S, Shakir S, Doblies J, et al. Early results of first versus second generation Amplatzer occluders for left atrial appendage closure in patients with atrial fibrillation. Clin Res Cardiol. Aug 2015; 104(8): 656-65. PMID 25736061
77. January CT, Wann LS, Calkins H, et al. 2019 AHA/ACC/HRS focused update of the 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. Heart Rhythm. Aug 2019; 16(8): e66-e93. PMID 30703530
78. Joglar JA, Chung MK, Armbruster AL, et al. 2023 ACC/AHA/ACCP/HRS Guideline for the Diagnosis and Management of Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. Jan 02 2024; 149(1): e1-e156. PMID 38033089
79. Gopinathannair R, Chen LY, Chung MK, et al. Managing Atrial Fibrillation in Patients With Heart Failure and Reduced Ejection Fraction: A Scientific Statement From the American Heart Association. Circ Arrhythm Electrophysiol. Jun 2021; 14(6): HAE0000000000000078. PMID 34129347
80. Saw J, Holmes DR, Cavalcante JL, et al. SCAI/HRS expert consensus statement on transcatheter left atrial appendage closure. Heart Rhythm. May 2023; 20(5): e1-e16. PMID 36990925