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# Surgical Left Atrial Appendage Occlusion Devices for Stroke Prevention in Atrial Fibrillation

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## Coverage

Surgical closure of the left atrial appendage, including excision and epicardial clipping (i.e., AtriClip™) **is considered not medically necessary** to reduce future stroke risk **except** when performed in conjunction with a Maze procedure for atrial fibrillation (AF).

## Policy Guidelines

None.

## Description

Atrial fibrillation (AF) is the most common type of cardiac arrhythmia. 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 one of the main goals of

AF treatment. Treatment with anticoagulant medications is a first-line approach to stroke prevention in individuals with AF, although occlusion of the left atrial appendage (LAA) may offer a non-pharmacological alternative to anticoagulant medications for those with a contraindication or intolerance to long-term anticoagulant use or with poor anticoagulant adherence. Multiple surgical techniques may be used to excise or occlude the LAA. One device, the AtriClip Left Atrial Appendage Exclusion System, has approval from the U.S. Food and Drug Administration for surgical LAA occlusion for stroke prevention in patients with AF.

**Atrial Fibrillation**

Nonvalvular AF is the most common type of cardiac arrhythmia, affecting at least 2.7 million people in the United States. The risk of AF has been found to be lower in Black, Hispanic, and Asian patients relative to White patients, following adjustment for demographic and AF risk factors. (1, 2) AF is typically described according to frequency and duration and includes paroxysmal (duration up to 1 week), persistent (>1 week), long-term persistent (>1 year), or permanent (normal sinus rhythm cannot be restored despite treatment). (3) Stroke is the most serious complication of AF. The estimated incidence of stroke in non-treated 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. (4, 5) Although this paradox may be partially attributable to clinical factors (e.g., congestive heart failure, hypertension, type 2 diabetes), Black and Hispanic patients with AF are less likely than White patients to receive stroke prevention therapy. (6) Stroke associated with AF is primarily thromboembolic, 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 AF treatment.

**Stroke Prevention**

The risk for stroke among patients with AF is evaluated using several factors. Two commonly used scores, the $CHADS_2$ score and the $CHA_2DS_2$-VASc score are described in Table 1:

**Table 1. $CHADS_2$ and $CHA_2DS_2$-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 years | 1 ($CHADS_2$)<br>2 ($CHA_2DS_2$-$VAS_c$) |
| 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 years | 1 |
| Sc | Sex category of female (female sex confers higher risk) | 1 |

Adapted from Lip et al. (2018) (7) and January et al. (2014). (8)

Stroke in AF occurs primarily as a result of thromboemboli from the left atrium. The erratic atrial contractions in AF lead to blood stasis in the left atrium, and this low flow state increases the risk for thrombosis. The first-line treatment for stroke prevention in AF is long-term anticoagulation, which has proven efficacy. (9) Warfarin, a vitamin K antagonist, is the predominant agent in clinical use. Several newer direct oral anticoagulant (DOAC) agents, 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. Warfarin requires frequent monitoring and adjustments as well as lifestyle changes; DOACs do not require the frequent monitoring seen with warfarin therapy. While anticoagulation is effective for stroke prevention, it carries an increased risk of bleeding. Reversal agents can be used to counter the effects of life-threatening bleeding in individuals using warfarin or DOAC therapy. Such agents carry their own risk of inducing life-threatening thrombosis. For individuals with AF who have a contraindication to warfarin and DOACs, dual antiplatelet therapy with aspirin and clopidogrel is an option for stroke prevention, though it is less protective than either warfarin or DOACs.

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). The LAA is a small extension of the left atrium that can vary widely in both size and shape (morphology). LAA morphologies are described according to their appearance and include: the chicken wing, which is the most common morphology and features a prominent bend in the dominant lobe; the cactus, characterized by a dominant central lobe with superior and inferior secondary lobes; the windsock, which features one dominant lobe; and the cauliflower, which is the least common morphology and features numerous lobes with none being dominant. It has been estimated that over 90% of left atrial thrombi occur in the LAA. Surgical removal or exclusion of the LAA is often performed in patients with AF who are undergoing open heart surgery. Surgical techniques to exclude the LAA include resection or occlusion through stapling or clipping. (9,10)

Percutaneous LAA occlusion is discussed in policy SUR701.009.

**Regulatory Status**

In June 2010, the AtriClip LAA Exclusion System (Atricure) was cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process (K093679). The FDA determined that this device was substantially equivalent to existing devices for occlusion of the LAA. The AtriClip has gone through numerous iterations since 2010, primarily relating to changes in the clip material composition and refinements of the clip applicator. The current FDA-cleared indication is unchanged from the original 2010 indication, which states that the

AtriClip is indicated for "exclusion of the LAA, performed under direct visualization, in conjunction with other cardiac surgical procedures." (11) The FDA clearance documentation notes that direct visualization “requires that the surgeon is able to see the heart directly, with or without assistance from a camera, endoscope, etc. or other appropriate viewing technologies." As of 2022, AtriCure markets 7 different versions of the AtriClip device, whose use varies according to LAA size and type of concomitant surgical procedure. (12)

## Rationale

Medical policies assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. Randomized controlled trials are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

**Surgical Left Atrial Appendage Occlusion Concomitant with an Open or Thoracoscopic Cardiac Procedure**

Clinical Context and Therapy Purpose

The purpose of surgical left atrial appendage (LAA) occlusion in association with an open or thoracoscopic cardiac procedure in individuals with atrial fibrillation (AF) at risk for embolic stroke is to provide a treatment option that is an alternative to or an improvement on existing therapies.

Use of anticoagulants is the first-line therapy for the reduction of the risk of stroke in individuals with AF. Surgical occlusion of the LAA with an occlusion device (e.g., AtriClip) may be a treatment option for those with contraindications or intolerance to anticoagulants, or in those with poor anticoagulant adherence.

The following PICO was used to select literature to inform this policy.

*Populations*
The relevant population(s) of interest are individuals with AF at increased risk for embolic stroke undergoing LAA occlusion concomitant with open or thoracoscopic cardiac surgical procedures.

*Interventions*
The therapy being considered is surgical LAA occlusion.

The efficacy of surgical LAA occlusion performed in conjunction with other cardiac procedures has been assessed in several systematic reviews and a large (N>10,000) observational study, which have generally found surgical LAA occlusion to be associated with a reduction in the risk of stroke or systemic embolism without an increased risk of post-procedural complications. (13-16)

*Comparators*
The following therapies are currently being used for the prevention of stroke in individuals with AF at increased risk for embolic stroke: anticoagulation therapy, other surgical LAA occlusion methods and no occlusion.

Warfarin is the predominant anticoagulant agent in clinical use. Several 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. Warfarin requires frequent monitoring and adjustments as well as lifestyle changes; direct oral anticoagulants (DOACs) do not require the frequent monitoring seen with warfarin therapy. While anticoagulation is effective for stroke prevention, it carries an increased risk of bleeding. Reversal agents can be used to counter the effects of life-threatening bleeding in individuals using warfarin or DOAC therapy. Such agents carry their own risk of inducing life-threatening thrombosis.

Surgical LAA occlusion methods other than the AtriClip device include epicardial stapling and excision and suture closure.

*Outcomes*
The general outcomes of interest are overall survival, morbid events, and treatment-related morbidity. The primary outcome of interest is the rate of ischemic stroke during follow-up, along with rates of systemic embolization, cardiac events, and mortality. Surgical success, defined as complete LAA occlusion, is not a direct health outcome, although evidence on surgical success is reported here as incomplete LAA occlusion, which may be associated with an increased risk of stroke. (17)

Follow-up of 6 to 12 months or longer is required to assess outcomes.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Consistent with a 'best available evidence approach,' within each category of study design, studies with larger sample sizes and longer durations were sought.
- Studies with duplicative or overlapping populations were excluded.

A number of studies were excluded from this medical policy because they did not specifically assess surgical LAA occlusion with the AtriClip device. (18, 21, 23-26)

Systematic Reviews

Toale et al. (2019) (27) conducted a systematic review assessing outcomes of LAA occlusion using the AtriClip device in individuals with AF either as a concomitant or stand-alone procedure. The review included 11 uncontrolled cohort studies and case series with a total population of 922 individuals (n ranged from 5 to 291; median n=40). Follow-up among the included studies ranged from time of hospital discharge to 4 years (median 1 year). Results from the largest studies (N>100) with the longest duration (>1 year) are discussed below (see Case Series section). The review found a surgical success rate of 97.8% (902/922) based on varying methods of assessing occlusion completion. When stratified according to surgical approach, success rates were slightly lower for AtriClip placement via a thoracoscopic approach (4 studies; 95.3%) than for an open approach (7 studies; 99.2%). This difference was statistically significant (p=.0002). At least one of the thoracoscopic studies (28) attributed their lower success rate to a learning curve associated with AtriClip placement (see Case Series, below). Within the 30-day postoperative period, 20 individuals underwent surgical revision due to bleeding, 4 had a postoperative ischemic stroke and there were 29 deaths. In follow-up greater than 6 months, there were 5 cases of ischemic stroke, and 42 deaths. Among 798 individuals with data, 477 (60%) had discontinued anticoagulant use.

Randomized Controlled Trials

Whitlock et al. (2021) (29) reported the results of The Left Atrial Appendage Occlusion Study (LAAOS) III that randomized 4,811 individuals to LAA occlusion or no occlusion scheduled to undergo cardiac surgery (Table 2). Following post-randomization exclusions prior to surgery, 2,379 individuals were included in the occlusion group and 2,411 were included in the no occlusion group (N=4,770). Demographic and clinical characteristics for the intervention and control groups were similar at baseline. Indications for cardiac surgery included isolated coronary artery bypass graft (CABG; 21%), isolated valve replacement (23%), or other cardiac surgical procedures (55%). Thirty-three percent of the enrolled population underwent surgical ablation for AF. Data on occlusion method were reported for 71% (1,685/2,379) of those randomized to the occlusion group. Occlusion method was selected by the treating surgeon.

Among those with data regarding the occlusion method, 15% underwent LAA occlusion with an epicardial closure device (e.g., AtriClip). The primary outcome was the incidence of ischemic stroke or systemic arterial embolism. The results of the trial are summarized in Table 3. At a mean 3.8 years follow-up, occlusion was associated with a significant reduction in risk of the primary outcome when compared with no occlusion, without an increased risk of post-procedural bleeding or mortality. Occlusion appeared to result in greater risk reduction among those using either DOAC (hazard ratio [HR], 0.54; 95% CI, 0.34 to 0.86) or vitamin K antagonist therapy (HR, 0.62; 95% CI, 0.39 to 1.00) at baseline than in those not on anticoagulant therapy (HR, 0.79; 95% CI, 0.56 to 1.12). Anticoagulant use was 83% in the occlusion group and 81% in the no occlusion group at the time of hospital discharge, and the majority of study participants in both groups continued to use anticoagulants at 1- (80% and 79%), 2- (77% and 78%), and 3-year follow-up (75% and 78%). There was no subgroup analysis by occlusion method. Reporting of harms after the perioperative period was limited, but the risk of a major bleeding event (HR, 0.93; 95% CI, 0.78 to 1.11), hospitalization for heart failure (HR, 1.13; 95% CI, 0.92 to 1.40), and myocardial infarction (HR, 0.82; 95% CI, 0.57 to 1.18) were similar between occlusion and no occlusion groups.

**Table 2. Summary of Key RCT Characteristics**

| **Study; Trial** | **Countries** | **Sites** | **Dates** | **Participants** | **Interventions** | |
|---|---|---|---|---|---|---|
| | | | | | *Surgical LAA Occlusion* | *No Surgical LAA Occlusion* |
| Whitlock et al. (2021) (29) LAAOS III | Multinational (27 countries in Asia, Australia, Europe, North America or South America) | 105 | 2012-2018 | Adults with a history of AF scheduled to undergo cardiac surgery with cardiopulmonary bypass and $CHA_2$-$DS_2$-VASc score ≥2<br>• Mean age 72 years<br>• 33% female<br>• Race/ethnicity NR<br>• Mean $CHA_2$-$DS_2$-VASc score 4.2<br>• 29% DOAC use; 23% | N=2,379 (15.1% epicardial clip [255/1685])[a] | N=2391 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | • vitamin K antagonist use<br>• 33% concomitant surgical ablation for AF | | |

AF: atrial fibrillation; DOAC: direct-acting oral anticoagulant; LAA: left atrial appendage; NR: not reported; RCT: randomized controlled trial.
[a]Data on occlusion method were reported for 1,685 (of 2,379) study participants.

**Table 3. Summary of Key RCT Results**

| Study | Ischemic Stroke or Systemic Atrial Embolism | Any Stroke | All-cause Mortality | Post-procedural Bleeding Requiring Reoperation[a] | Post-procedural Mortality (≤30 days) |
|---|---|---|---|---|---|
| **Whitlock et al. (2021) (29) LAAOS III** | N=4770 | N=4770 | N=4770 | N=4770 | N=4770 |
| Occlusion | 114/2379 (4.8%) | 113/2379 (4.7%) | 538/2379 (22.6%) | 94/2379 (4.0%) | 89/2379 (3.7%) |
| No occlusion | 168/2391 (7.0%) | 176/2391 (7.4%) | 537/2391 (22.5%) | 95/2391 (4.0%) | 95/2391 (4.0%) |
| NR/Diff/RR (95% CI) | HR 0.67 (0.53 to 0.85) | HR 0.63 (0.50 to 0.80) | HR 1.00 (0.89 to 1.13) | RR 0.99 (0.75 to 1.32) | RR 0.94 (0.71 to 1.25) |

CI: confidence interval; HR: hazard ratio; RCT: randomized controlled trial; RR: relative risk.
[a]Reoperation within 48 hours of initial surgery

Study relevance and design and conduct limitations are summarized in Tables 4 and 5. The purpose of the study limitations tables is to display notable limitations identified in each study. This information is synthesized as a summary of the body of evidence following each table and provides the conclusions on the sufficiency of evidence supporting the position statement.

The LAAOS III trial had some other important limitations not captured in Tables 4 and 5. Only 15% underwent LAA occlusion with an epicardial closure device (e.g., AtriClip). No subgroup analysis was conducted according to occlusion method. According to the study's authors, this was due to the lack of randomization for occlusion method. Consequently, the study authors noted "we cannot discern from our results whether all surgical closure methods are

comparable" and no conclusions about the effectiveness of AtriClip placement relative to other occlusion methods can be drawn from the trial. In addition, due to the lack of an anticoagulant control group, no conclusions can be drawn from the trial about the comparative effectiveness of AtriClip versus first-line therapy (anticoagulants). The fact that 75% or more of study participants were still using anticoagulants up to 3 years following LAA occlusion also limits the applicability of the study results for those individuals with AF and a contraindication to anticoagulant use.

**Table 4. Study Relevance Limitations**

| Study | Population[a] | Intervention[b] | Comparator[c] | Outcomes[d] | Duration of Follow-up[e] |
|---|---|---|---|---|---|
| Whitlock et al. (2021) (29) LAAOS III | 5. Race/ethnicity not reported | 2. No stratified analysis according to occlusion method | | | |

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a]Population key: 1. Intended use population unclear; 2. Study population is unclear; 3. Study population not representative of intended use; 4, Enrolled populations do not reflect relevant diversity; 5. Other.
[b]Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest (e.g., proposed as an adjunct but not tested as such); 5: Other.
[c]Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively; 5. Other.
[d]Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. Incomplete reporting of harms; 4. Not establish and validated measurements; 5. Clinically significant difference not prespecified; 6. Clinically significant difference not supported; 7. Other.
[e]Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms; 3. Other.

**Table 5. Study Design and Conduct Limitations**

| Study | Allocation[a] | Blinding[b] | Selective Reporting[c] | Data Completeness[d] | Power[e] | Statistical[f] |
|---|---|---|---|---|---|---|
| Whitlock et al. (2021) (29) LAAOS III | | | | | | |

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a]Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias; 5. Other.
[b]Blinding key: 1. Participants or study staff not blinded; 2. Outcome assessors not blinded; 3. Outcome assessed by treating physician; 4. Other.

[c]Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication; 4. Other.
[d]Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials); 7. Other.
[e]Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference; 4. Other.
[f]Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated; 5. Other.

The AtriClip® Left Atrial Appendage Exclusion Concomitant to Structural Heart Procedures (ATLAS) RCT compared the AtriClip device (n=376) with medical management (standard of care anticoagulant therapy; n=186) in individuals undergoing a valve or CABG procedure. (30) The study population did not have a history of AF, but had CHA2DS2-VASc of 2 or more (mean score, 3.4). The study completion date was June 2019. Full study results have not been published, but some 1 year results have been reported on ClinicalTrials.gov. Rates of postoperative AF were similar between AtriClip (47.3%) and medical management (40.3%) groups. Rates were also similar between groups (8.5% vs. 8.6%) for a composite outcome that included thromboembolic and hemorrhagic events (e.g., ischemic or hemorrhagic stroke, transient ischemic attack [TIA], peripheral ischemia, bleeding event). The rate of all-cause mortality in the AtriClip group (5.32%) was more than double that in the medical management group (2.15%). Full publication of these results would provide direct evidence on the effectiveness of AtriClip versus standard of care management with anticoagulation therapy.

*Nonrandomized studies*
A retrospective database study conducted by Soltesz et al. (2021) (31) compared outcomes in 931 Medicare patients who underwent concomitant CABG and LAA occlusion with AtriClip with 3,279 patients who underwent CABG only without AtriClip placement (Table 6). The study was funded by the AtriClip manufacturer and was designed to assess both health outcomes and resource utilization. Anticoagulant use was not reported and it is unclear if baseline use was similar between the 2 groups. Surgical LAA occlusion with AtriClip was associated with a lower risk of thromboembolism, and a nonsignificant reduction in risk of ischemic stroke. There was no difference between AtriClip occlusion and no occlusion groups in post-surgical mortality (≤90 days), but LAA occlusion with AtriClip was associated with a lower risk of death at 90 days or more post-surgery (Table 7).

**Table 6. Summary of Key Observational Comparative Studies**

| Study | Study Type | Country | Dates | Participants | Surgical LAA Occlusion | Non Surgical LAA Occlusion | Follow-Up |
|---|---|---|---|---|---|---|---|
| Soltesz et al. | Registry | U.S. | 2015-2017 | N=4,210 | N=931 | N=3279 | 2 years |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| (2021) (31) | | | | Individuals age ≥65 years included in a Medicare database with AF who underwent concomitant isolated CABG (without ablation)<br>• Mean age 74 years<br>• 26% female<br>• Mean $CHA_2$-$DS_2$-VASc score 3.6 | Surgical LAA occlusion with the AtriClip device | | |

AF: atrial fibrillation; CABG: coronary artery bypass graft; LAA: left atrial appendage; U.S.: United States.

**Table 7. Summary of Key Observational Comparative Study Results**

| Study | Ischemic Stroke[a] | Thromoembolism[a] | Mortality, 0-90 Days | Mortality, 91-730 Days[a] |
|---|---|---|---|---|
| **Soltesz et al. (2021) (31)** | N=4,210 | N=4,210 | N=4,210 | N=4,210 |
| Surgical LAA occlusion with AtriClip | 2.3% | 4.4% | NR | 3.7% |
| No surgical LAA occlusion | 3.1% | 5.9% | NR | 6.9% |
| HR (95% CI) | sHR 0.74 (0.49 to 1.11) | sHR 0.74 (0.54 to 1.00) | HR 1.05 (0.79 to 1.40) | HR 0.55 (0.32 to 0.95) |

CI: confidence interval; HR: hazard ratio; NR: not reported; sHR: subhazard ratio
[a]Proportions represent annual risk, not absolute event rates

*Case Series*

As noted above, the 2019 Toale et al. (27) systematic review included 11 uncontrolled cohort) included more than 100 individuals who had AtriClip placement concomitant to cardiac surgery with follow-up of a year or more (Table 8). Both studies found AtriClip placement associated with successful occlusion rates of 98% or greater and stroke rates of 1% or fewer in the postoperative period and 2% or fewer in the long-term follow-up (Table 9). Kurfirst et al (2017) (33) attributed their less than 100% success rate to a learning curve associated with AtriClip placement; 2 of the 3 failures were among the first 10 cases receiving AtriClip placement. An additional case series published by Heijden et al. (2022) was identified, which included 119 individuals with AF treated by minimally invasive thoracoscopic epicardial ablation; the majority of patients were occluded with Atriclip (n=103; 90%), but the remaining patients were occluded with a different device (Lariat, Watchman, or stapler) or were not occluded due to

complifrications. (34) No stroke or mortality occurred post-operatively or through 2 years of follow-up (Table 9).

**Table 8. Summary of Key Case Series Characteristics**

| Study | Country | Participants | Follow-Up |
|---|---|---|---|
| Caliskan et al. (2018) (32) | U.S., Switzerland, Germany | N=291<br>Individuals with AF undergoing cardiac surgery<br>• Mean age 71 years<br>• 32% female<br>• Mean $CHA_2$-$DS_2$-VASc score 3.1<br>• 67% DOAC use<br>• 20% isolated CABG; 22% combined CABG and valve procedure; 42% single or multiple valve procedures<br>• 67% surgical ablation | 3 years |
| Kurfirst et al. (2017) (33) | Czech Republic | N=155[a]<br>• Mean age 67 years<br>• 34% female<br>• Mean $CHA_2$-$DS_2$-VASc score 2.7<br>• Anticoagulant use NR<br>• 25% valve procedure; 21% CABG; 4% combined procedure<br>• 46% thoracoscopic ablatio | 2 years |
| Heijden et al. (2022) (34) | The Netherlands, Belgium | N=119[b]<br>• Mean age 64 years<br>• 28% female<br>• Mean $CHA_2$-$DS_2$-VASc score 2<br>• Anticoagulant use NR<br>• unilateral left-sided, minimally invasive bilateral thoracoscopic epicardial ablation; 100% | 2 years |

AF: atrial fibrillation; CABG: coronary artery bypass graft; DOAC: direct-acting oral anticoagulants; NR: not reported.

[a]4.5% (7/155) underwent AtriClip placement as a stand-alone procedure

[b]A minority of the patients (10%) utilized an occlusion device other than Atriclip. These devices includedincluded: Lariat (n=4), stapler (n=2), Watchman device (n=6) and no closure due to complications (n=5).

**Table 9. Summary of Key Case Series Results**

| Study | Successful Occlusion | Continued Anticoag-ulant Use | Stroke | Mortality | Post-procedural Adverse Events | >30 Day Adverse Events |
|---|---|---|---|---|---|---|
| Caliskan et al. (2018) (32) | 291/291 (100%) | 109/275 (39.6%) | Post-operative (in hospital): 3/291 (1.0%)<br><br>Follow-up: 2/291 (1.7%) | Post-operative (in hospital): 18/291 (6.2%)<br><br>Follow-up: 36/291 (12.4%) | 0/291 (0%) | 0/291 (0%) |
| Kurfirst et al. (2017) (33) | 152/155 (98.0%) | Anti-coagulant or anti-platelet use: 75/142 (52.8%) | Post-operative (in hospital): 1/155 (0.6%)<br><br>Follow-up: 1/155 (0.7%) | Post-operative (in hospital): 13/155 (8.4%)<br><br>Follow-up: NR | Revision due to bleeding: 10/155 (6.4%) | NR |
| Heijden et al. (2022) (34) | NR | NR | Post-operative (in hospital): 0/119 (0%)<br><br>Follow-up 0/119 (0%) | Post-operative (in hospital): 0/119 (0%)<br><br>Follow-up 0/119 (0%) | Revision due to bleeding: 1(0.8%)<br>Cardiac tamponade: 1(0.8%)<br>Myocardial Infarction: 1(0.8%)<br>Pacemaker implantation 1(0.8%)<br>Pneumothorax: 1(0.8%)<br>Minor complications: 6(5%) | Follow-up through 24 months:<br>Late cardiac tamponade: 2(1.7%)<br>diaphragm paresis: 1 (0.8%)<br>hemothorax: 1 (0.8%)<br>Pacemaker or cardioverter-defibrillator implantation: 3 (2.5%)<br>Pericarditis requiring medication: 4 (3.4%) |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | | | Pericardiocentesis: 2(1.7%)<br>Pleural effusion: 2 (1.7%)<br>Pneumonia: 1 (0.8%)<br>Hospital readmission due to decompensation cordis: 2 (1.7%) |

NR: not reported.

Observational Studies

Friedman et al. (2018) performed a retrospective cohort study in order to evaluate the association of surgical left atrial appendage occlusion (S-LAAO) for reducing the risk of thromboembolism. (16) Participants included patients aged 65 years and older with AF undergoing cardiac surgery (coronary artery bypass grafting [CABG], mitral valve surgery with or without CABG, or aortic valve surgery with or without CABG) with and without concomitant S-LAAO. The primary outcome was readmission for thromboembolism (stroke, transient ischemic attack, or systemic embolism) at up to 3 years of follow-up. Secondary end points included hemorrhagic stroke, all-cause mortality, and a composite end point (thromboembolism, hemorrhagic stroke, or all-cause mortality). Among 10,524 patients undergoing surgery (median age, 76 years; 39% female; median CHA2DS2-VASc score, 4), 3,892 (37%) underwent S-LAAO. Overall, at a mean follow-up of 2.6 years, thromboembolism occurred in 5.4%, hemorrhagic stroke in 0.9%, all-cause mortality in 21.5%, and the composite end point in 25.7%. S-LAAO, compared with no S-LAAO, was associated with lower unadjusted rates of thromboembolism (4.2% vs 6.2%), all-cause mortality (17.3% vs 23.9%), and the composite end point (20.5% vs 28.7%) but no significant difference in rates of hemorrhagic stroke (0.9% vs 0.9%). After inverse probability-weighted adjustment, S-LAAO was associated with a significantly lower rate of thromboembolism (subdistribution hazard ratio [HR], 0.67; 95% CI, 0.56-0.81; P < .001), all-cause mortality (HR, 0.88; 95% CI, 0.79-0.97; P = .001), and the composite end point (HR, 0.83; 95% CI, 0.76-0.91; P < .001) but not hemorrhagic stroke (subdistribution HR, 0.84; 95% CI, 0.53-1.32; P = .44). S-LAAO, compared with no S-LAAO, was associated with a lower risk of thromboembolism among patients discharged without anticoagulation (unadjusted rate, 4.2% vs 6.0%; adjusted subdistribution HR, 0.26; 95% CI, 0.17-0.40; P < .001), but not among patients discharged with anticoagulation (unadjusted rate, 4.1% vs 6.3%; adjusted subdistribution HR, 0.88; 95% CI, 0.56-1.39; P = .59). The authors concluded that among older patients with AF undergoing concomitant cardiac surgery, S-LAAO, compared with no S-LAAO, was associated with a lower risk of readmission for thromboembolism over 3 years. These findings support the use of S-LAAO, but randomized trials are necessary to provide definitive evidence.

**Section Summary: Surgical Left Atrial Appendage Occlusion Concomitant With an Open or Thoracoscopic Cardiac Procedure**

Evidence comparing surgical LAA occlusion with anticoagulation, another surgical occlusion method, or no occlusion in individuals undergoing concomitant cardiac procedures is limited. LAA occlusion was associated with a reduced risk of stroke versus no occlusion in the LAAOS III trial. An industry-sponsored retrospective database study that compared LAA occlusion with AtriClip with no occlusion found that AtriClip placement was associated with a lower risk of ischemic stroke and a reduced risk of thromboembolism. Large (N>100) case series with 2- to 3-years follow-up reported stroke rates 1% or fewer in the postoperative period and 2% or fewer in the long-term follow-up. A large study that evaluated the association of surgical left atrial appendage occlusion (S-LAAO) for reducing the risk of thromboembolism concluded that among older patients with AF undergoing concomitant cardiac surgery, S-LAAO, compared with no S-LAAO, was associated with a lower risk of readmission for thromboembolism over 3 years. Secondary end points included decreases in hemorrhagic stroke, all-cause mortality, and a composite end point (thromboembolism, hemorrhagic stroke, or all-cause mortality).

**Surgical Left Atrial Appendage Excision Concomitant with an Open or Thoracoscopic Cardiac Procedure**

Clinical Context and Therapy Purpose

The purpose of surgical left atrial appendage (LAA) excision in association with an open or thoracoscopic cardiac procedure in individuals with atrial fibrillation (AF) at risk for embolic stroke is to provide a treatment option that is an alternative to or an improvement on existing therapies.

Use of anticoagulants is the first-line therapy for the reduction of the risk of stroke in individuals with AF. Surgical excision of the LAA may be a treatment option for those with contraindications or intolerance to anticoagulants, or in those with poor anticoagulant adherence.

The following PICO was used to select literature to inform this policy.

*Populations*

The relevant population(s) of interest are individuals with AF at increased risk for embolic stroke undergoing LAA excision concomitant with open or thoracoscopic cardiac surgical procedures.

*Interventions*

The therapy being considered is surgical LAA excision.

*Comparators*

The following therapies are currently being used for the prevention of stroke in individuals with AF at increased risk for embolic stroke: anticoagulation therapy, other surgical LAA occlusion methods and no occlusion.

Warfarin is the predominant anticoagulant agent in clinical use. Several 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. Warfarin requires frequent monitoring and adjustments as well as lifestyle changes; direct oral anticoagulants (DOACs) do not require the frequent monitoring seen with warfarin therapy. While anticoagulation is effective for stroke prevention, it carries an increased risk of bleeding. Reversal agents can be used to counter the effects of life-threatening bleeding in individuals using warfarin or DOAC therapy. Such agents carry their own risk of inducing life-threatening thrombosis.

*Outcomes*

The general outcomes of interest are overall survival, morbid events, and treatment-related morbidity. The primary outcome of interest is the rate of ischemic stroke during follow-up, along with rates of systemic embolization, cardiac events, and mortality. Surgical success, defined as complete LAA excision, is not a direct health outcome, although evidence on surgical success is reported here as incomplete LAA excision, which may be associated with an increased risk of stroke. (17)

Follow-up of 6 to 12 months or longer is required to assess outcomes.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Consistent with a 'best available evidence approach,' within each category of study design, studies with larger sample sizes and longer durations were sought.
- Studies with duplicative or overlapping populations were excluded.

Randomized Controlled Trials

Jiang et al. (2020) conducted a RCT to study evaluate the role of surgical left atrial appendage (LAA) exclusion in the prevention of stroke after mitral valve replacement (MVR). (22) retrospectively reviewed clinical data of 860 patients who received MVR in our center from January 2008 to January 2013. The patients were randomly assigned to two surgical groups, namely LAA exclusion group (n = 521) and LAA nonexclusion group (n = 339) according to whether concurrent surgical exclusion of the LAA was to be undertaken or not before surgery in a blind fashion. MVR was performed by two experienced surgeons. The LAA was explored during the operation and mural thrombus removed in all cases. The LAA was left intact in nonocclusion group whereas the neck of the LAA was closed with a two-layer continued suture in exclusion group. The incidence of early postoperative ischemic stroke between the two groups was compared. The patients' age was 53 ± 12 years, with 48.1% male and 67.9% with

rheumatic disease. Mural thrombosis was seen in 18.8% of the patients and atrial fibrillation (AF) coexisted in 62.4%. All operations were successfully performed, and no difference was noted in in-hospital mortality, re-exploration for bleeding, and other major complications between the two groups. The incidence of ischemic stroke in LAA exclusion group was significantly lower than in nonexclusion group (0.6% vs. 2.7%, p = .011). The subgroup multivariate analysis showed that LAA exclusion significantly reduced the risk of postoperative stroke in patients with AF (odds ratio [OR] = 0.070, 95% confidence interval [CI]: 0.006-0.705, p = .025) but not in non-AF patients (OR = 1.902, 95% CI: 0.171-21.191, p = .601). In conclusion the study found concurrent LAA exclusion during MVR is a safe and effective way to reduce postoperative ischemic stroke, particularly in patients with AF.

Other Studies

Blackshear et al. (2023) evaluated left atrial appendage obliteration in high-risk patients with atrial fibrillation (AF). (19) Left atrial appendage thrombosis and embolization is the principal mechanism of stroke in AF. Thoracoscopic Left Appendage, Total Obliteration, No cardiac Invasion (LAPTONI) was undertaken with a loop snare in eight patients and a stapler in seven patients, median age 71 years, with clinical risk factors for stroke and with an absolute contraindication to or failure of prior thrombosis prevention with warfarin. Eleven patients had a history of prior thromboembolism. One patient took sustained warfarin during follow-up. The LAPTONI procedure was completed in 14 of 15 patients, and 1 patient required urgent conversion to open thoracotomy because of bleeding. Patients have been followed up for 8 to 60 months, mean 42 +/- 14 months. One fatal stroke occurred 55 months after surgery, and one non-disabling stroke three months after surgery. Two other deaths occurred, one after coronary bypass surgery and the other from hepatic failure. The subgroup of 11 patients with prior thromboembolism had an annualized rate of stroke of 5.2% per year (95% confidence interval [CI] 1.3 to 21) after LAPTONI, which compares to a rate of 13% per year (95% CI 9.0 to 19) for similar aspirin-treated patients from the Stroke Prevention in Atrial Fibrillation trials (p = 0.15). The LAPTONI procedure appears technically feasible without immediate disabling neurologic morbidity or mortality although rates of post-op complications remain high.

Melduni et al. (2017) evaluated 9,792 adults who underwent coronary artery bypass grafting and valve surgery between January 2000 and December 2005. (40) A propensity score-matching analysis based on 28 pretreatment covariates was performed and 461 matching pairs were derived and analyzed to estimate the association of LAA closure with early postoperative atrial fibrillation (POAF) (AF ≤30 days of surgery), ischemic stroke, and mortality. In the propensity-matched cohort, the overall incidence of POAF was 53.9%. In this group, the rate of early POAF among the patients who underwent LAA closure was 68.6% versus 31.9% for those who did not undergo the procedure (P<0.001). LAA closure was independently associated with an increased risk of early POAF (adjusted odds ratio [OR], 3.88; 95% CI, 2.89–5.20), but did not significantly influence the risk of stroke (adjusted HR, 1.07; 95% CI, 0.72–1.58) or mortality (adjusted HR, 0.92; 95% CI, 0.75–1.13). Researchers concluded after adjustment for treatment allocation bias, that LAA closure during routine cardiac surgery was significantly associated with an increased risk of early POAF, but it did not influence the risk of stroke or mortality. It remains uncertain

whether prophylactic exclusion of the LAA is warranted for stroke prevention during non–atrial fibrillation-related cardiac surgery.

Fu et al. (2019) set out to assess the safety and efficacy of thoracoscopic LAA occlusion for stroke prevention in patients with nonvalvular atrial fibrillation compared with long-term warfarin therapy. (20) Four hundred and ninety-two nonvalvular atrial fibrillation patients were enrolled. Two hundred and fifty-seven patients were treated with thoracoscopic LAA occlusion and 235 with long-term warfarin therapy. At 24 months, the rate of the first efficacy endpoint (composite of stroke, systemic embolism, and death) was 0.018 in the surgical group versus 0.043 in the warfarin group (p = 0.033). The rate of the second efficacy endpoint (stroke and systemic embolism excluding the first 7 days after procedure) was 0.010 versus 0.034 (p = 0.019). The rate of the first safety endpoint of bleeding was 0.016 versus 0.044 (p = 0.022). In conclusion, this study showed that thoracoscopic LAA occlusion was superior to warfarin for stroke prevention. The surgical group also had significantly lower bleeding risk.

**Section Summary: Surgical Left Atrial Appendage Excision Concomitant with an Open or Thoracoscopic Cardiac Procedure**
Randomized controlled trial evidence comparing surgical LAA excision with anticoagulation, another surgical occlusion method, or no occlusion in individuals undergoing concomitant cardiac procedures is limited. Other studies did show lower risks of atrial fibrillation, ischemic stroke and mortality. Results showed significantly fewer thromboembolic events in the group undergoing LAA excision compared with the group receiving medication alone.

**Surgical Left Atrial Appendage Occlusion as a Stand-Alone Procedure**
Clinical Context and Therapy Purpose
The purpose of surgical LAA occlusion in individuals with AF at risk for embolic stroke is to provide a treatment option that is an alternative to or an improvement on existing therapies.

As noted above, use of anticoagulants is the first-line therapy for the reduction of the risk of stroke in individuals with AF. Surgical occlusion of the LAA with AtriClip may be a treatment option for those with contraindications or intolerance to anticoagulants, or in those with poor anticoagulant adherence.

The following PICO was used to select literature to inform this policy.

*Populations*
The relevant population(s) of interest is individuals with AF at increased risk for embolic stroke undergoing LAA occlusion as a stand-alone procedure.

*Interventions*
The therapy being considered is surgical LAA occlusion.

The efficacy of surgical LAA occlusion performed in conjunction with other cardiac procedures has been assessed in several systematic reviews and a large (N>10,000) observational study,

which have generally found surgical LAA occlusion to be associated with a reduction in the risk of stroke or systemic embolism without an increased risk of post-procedural complications. (14) This review focuses on surgical LAA occlusion with AtriClip. This review does not consider the net health benefit of surgical LAA occlusion in general, nor does it address the net health benefit of surgical LAA occlusion techniques other than AtriClip placement.

*Comparators*
The following therapies are currently being used for the prevention of stroke in individuals with AF at increased risk for embolic stroke: anticoagulation therapy or percutaneous LAA occlusion.

Warfarin is the predominant anticoagulant agent in clinical use. Several newer anticoagulant medications, including dabigatran, rivaroxaban apixaban, and edoxaban have received U.S. FDA approval for stroke prevention in nonvalvular AF and have demonstrated noninferiority to warfarin in clinical trials. Warfarin requires frequent monitoring and adjustments as well as lifestyle changes; DOACs do not require the frequent monitoring seen with warfarin therapy. While anticoagulation is effective for stroke prevention, it carries an increased risk of bleeding. Reversal agents can be used to counter the effects of life-threatening bleeding in individuals using warfarin or DOAC therapy. Such agents carry their own risk of inducing life-threatening thrombosis.

Percutaneous LAA occlusion devices have been developed as a nonpharmacologic alternative for stroke prevention in AF. These devices are delivered through a catheter guided by transesophageal echocardiography or fluoroscopy. Percutaneous LAA occlusion requires the use of anticoagulation therapy during the perioperative period, followed by antiplatelet therapy. Percutaneous LAA occlusion devices are further discussed in policy 701.009.

*Outcomes*
The general outcomes of interest are overall survival, morbid events, and treatment-related morbidity. The primary outcome of interest is the rate of ischemic stroke during follow-up, along with rates of systemic embolization, cardiac events, and mortality. Surgical success, defined as complete LAA occlusion, is not a direct health outcome, although evidence on surgical success is reported here as incomplete LAA occlusion may be associated with an increased risk of stroke. (17)

Follow-up of 6 to 12 months or longer is required to assess outcomes.

<u>Study Selection Criteria</u>
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.

- Consistent with a 'best available evidence approach,' within each category of study design, studies with larger sample sizes and longer durations were sought.
- Studies with duplicative or overlapping populations were excluded.

Nonrandomized Studies

Branzoli et al. (2022) (35) conducted a retrospective cohort study of 40 individuals with AF and a contraindication to anticoagulant use managed by a Heart Team. Participants had a mean age of 74 years, 35% were female and had a mean CHA2DS2VASc score of 5.1 at baseline. Between 2017 and 2020, 20 individuals underwent surgical (thoracoscopic) LAA occlusion with the AtriClip device and 20 received percutaneous LAA occlusion with the Watchman device. Perioperative outcomes (procedure duration, length of hospital stay) were similar between groups with no serious adverse events or deaths. At a mean follow-up of 33 months, there were no instances of hospitalization due to cardiovascular or neurological events in either group.

Case Series

Cartledge et al. (2022) (36) and Franciulli et al. (2020) (37) reported on the use of AtriClip as a stand-alone LAA occlusion procedure in individuals at high-risk of stroke (Table 10). In both studies, AtriClip placement was achieved via a thoracoscopic approach. LAA occlusion was successful in nearly all cases, with few post-procedural events. No incidence of stroke was reported in either study after 6-months or 1-year follow-up (Table 11). There were 6 deaths in the Cartledge et al. study after 1 year, but the study authors deemed none device or procedure related.

**Table 10. Summary of Key Case Series Characteristics**

| Study | Country | Participants | Follow-Up |
|---|---|---|---|
| Cartledge et al. 2022 (36) | U.S., Poland | N=175<br>Individuals with AF at high-risk of stroke with a contraindication to anticoagulants (intolerance or failure) who were not candidates for ablation or other cardiac procedures<br>• Mean age not reported; 51% ≥75 years<br>• 49% female<br>• Mean $CHA_2$-$DS_2$-VASc score 4.0<br>• 78% history of bleeding; 26% prior stroke or TIA<br>• 66% oral anticoagulant or low molecular weight heparin | 1 year |

| | | | |
|---|---|---|---|
| Franciulli et al. 2020 (37) | Italy | N=20<br>Individuals with AF at high bleeding risk evaluated by a Heart Team<br>• Mean age 75 years<br>• 20% female<br>• Mean $CHA_2$-$DS_2$-VASc score 3.6<br>• 30% prior ischemic stroke | 6 months |

AF: atrial fibrillation; TIA: transient ischemic attack; U.S.: United States.

**Table 11. Summary of Key Case Series Results**

| Study | Successful Occlusion | Anticoagulant Use | Stroke | Mortality | Post-procedural Adverse Events | >30-day Adverse Events |
|---|---|---|---|---|---|---|
| Cartledge et al. 2022 (36) | 174/175 (99.4%) | 22/173 (12.7%) Oral anticoagulant or low molecular weight heparin at time of hospital discharge | No events | 6/165 (3.6%) | 1/173 (0.6%) Acute heart failure<br><br>1/173 (0.6%) Hemorrhagic stroke | No major bleeding events, device migration or intercardiac thrombi in the area of the occluder reported |
| Franciulli et al. 2020 (37) | 20/20 (100.0%) | NR | 0/20 (0%) | 0/20 (0%) | 1/20 (5.0%) Reoperation due to bleeding | NR |

NR: not reported.

Section Summary: Surgical Left Atrial Appendage Occlusion as a Stand-Alone Procedure

Evidence on surgical LAA occlusion as a stand-alone procedure is limited. One small (N=40) retrospective observational study found use of AtriClip as a stand-alone procedure resulted in similar outcomes as percutaneous LAA occlusion; the evidence is too limited to draw definitive conclusions. Well-designed RCTs with follow-up of 1 year or more comparing AtriClip LAA occlusion with anticoagulants or percutaneous LAA occlusion are needed to provide adequate evidence for the assessment of net health benefit. The ongoing SALAMANDER study (NCT05144958; completion anticipated in 2025) should provide direct comparative evidence of stand-alone AtriClip LAA occlusion with percutaneous occlusion when published.

**Summary of Evidence**

For individuals with atrial fibrillation (AF) at increased risk for embolic stroke undergoing left atrial appendage (LAA) occlusion concomitant with open or thoracoscopic cardiac surgical procedures, the evidence includes randomized controlled trials (RCTs), controlled observational studies, systemic reviews, nonrandomized studies and case series. Relevant outcomes are ischemic stroke, cardiac events, and mortality. LAA occlusion was associated with a reduced risk of stroke versus no occlusion in the Left Atrial Appendage Occlusion Study (LAAOS) III trial. A retrospective database study that compared the AtriClip device with no occlusion found that AtriClip placement was associated with a lower risk of ischemic stroke and a reduced risk of thromboembolism. Another large study that evaluated the association of surgical left atrial appendage occlusion (S-LAAO) for reducing the risk of thromboembolism concluded that among older patients with AF undergoing concomitant cardiac surgery, S-LAAO, compared with no S-LAAO, was associated with a lower risk of readmission for thromboembolism over 3 years. Secondary end points included decreases in hemorrhagic stroke, all-cause mortality, and a composite end point (thromboembolism, hemorrhagic stroke, or all-cause mortality).The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

For individuals with atrial fibrillation (AF) at increased risk for embolic stroke undergoing left atrial appendage (LAA) excision concomitant with open or thoracoscopic cardiac surgical procedures, the evidence includes a randomized controlled study, 2 matched cohort studies and a multicenter study. The relevant outcomes are overall survival, morbid events, and treatment-related morbidity. LAA excision patients showed lower incidences of ischemic stroke than in nonexclusion group. Studies found concurrent LAA exclusion during MVR is a safe and effective way to reduce postoperative ischemic stroke, particularly in patients with AF. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

For individuals with AF at increased risk for embolic stroke undergoing LAA occlusion as a stand-alone procedure (i.e., not performed in conjunction with a Maze procedure for AF) the evidence includes a controlled observational study and case series. Relevant outcomes are ischemic stroke, cardiac events, and mortality. One small (N=40) industry-sponsored retrospective observational study reported that use of the AtriClip device as a stand-alone procedure resulted in similar outcomes compared to percutaneous LAA occlusion. This evidence is too limited to draw definitive conclusions. Further research, including that from RCTs, is needed to more definitively determine the role of surgical LAAC as a stand alone procedure. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

**Practice Guidelines and Position Statements**

American Heart Association et al.

In 2019, the American Heart Association, in conjunction with the American College of Cardiology and the Heart Rhythm Society, issued a focused update of their 2014 joint guideline on the management of individuals with atrial fibrillation (AF). (38) The focused update states that "surgical occlusion of the LAA may be considered in patients with AF undergoing cardiac

surgery as a component of an overall heart team approach to the management of AF" (Class IIB [weak evidence of benefit outweighing risk]; Level B-NR [moderate-quality evidence from nonrandomized studies or meta-analyses of those studies]). No recommendation was made regarding the method of surgical LAA occlusion.

Society for Cardiovascular Angiography & Interventions et al.

In 2023, the Society for Cardiovascular Angiography & Interventions (SCAI) and Heart Rhythm Society (HRS) issued a consensus statement on transcatheter endovascular left atrial appendage closure (LAAC). (39) The following are the recommendations on patient selection and physician experience prior to receiving or performing LAAC:

- Transcatheter LAAC is appropriate for patients with nonvalvular atrial fibrillation with high thromboembolic risk who are not suited for long-term oral anticoagulation and who have adequate life expectancy (minimum >1 year) and quality of life to benefit from LAAC. There should be patient-provider discussion for shared decision making.
- Physicians performing LAAC should have a prior experience, including 50 or more prior left-sided ablations or structural procedures and 25 or more transseptal punctures (TSPs). Interventional imaging physicians should have experience in guiding 25 or more TSPs before supporting any LAAC procedures independently.

No recommendation was made regarding the method of surgical LAA occlusion.

American College of Chest Physicians

Guidance from the American College of Chest Physicians in 2018 (7) recommends:

- In patients with AF at high risk of ischemic stroke who have absolute contraindications for oral anticoagulants (OAC), we suggest using LAA occlusion (weak recommendation, low quality evidence).
- In AF patients at risk of ischemic stroke undergoing cardiac surgery, we suggest considering surgical exclusion of the LAA for stroke prevention, but the need for long-term OAC is unchanged (weak recommendation, low quality evidence).

No guideline statement recommends a specific occlusion method or approach.

**Ongoing and Unpublished Clinical Trials**

Some currently ongoing and unpublished trials that might influence this policy are listed in Table 12.

**Table 12. Summary of Key Trials**

| NCT Number | Trial Name | Planned Enrollment | Completion Date |
|---|---|---|---|
| **Ongoing** | | | |
| NCT05101993 | VClip Post-Market Study | 156 | Aug 2023 |
| NCT05144958 | Stand-Alone Left Atrial Appendage Occlusion for throMboembolism Prevention in Nonvalvular Atrial | 400 | Mar 2025 |

| | | | |
|---|---|---|---|
| | fibrillatioN DiseasE Registry (SALAMANDER) | | |
| NCT03838341 | Stand-Alone Thoracoscopic Epicardial Left Atrial Appendage Occlusion With AtriClip® Device for Thromboembolism Prevention in Nonvalvular Atrial Fibrillation - the Polish Nationwide Registry. | 100 | Jan 2025 |
| NCT05723536 | PLAI-AF Trial: Hybrid Endo-epicardial Partial Left Atrial Isolation vs. Endocardial Ablation in Patients With Persistent Atrial Fibrillation (PLAI-AF) | 80 | Dec 2025 |
| NCT05478304 | Left Atrial Appendage Exclusion for Prophylactic Stroke Reduction Trial | 6500 | Apr 2032 |
| **Unpublished** | | | |
| NCT02701062[a] | | 562 | Jun 2019 |

NCT: national clinical trial.

[a]Denotes industry-sponsored or cosponsored trial

## Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

| | |
|---|---|
| **CPT Codes** | 33267, 33268, 33269 |
| **HCPCS Codes** | None |

*Current Procedural Terminology (CPT®) ©2023 American Medical Association: Chicago, IL.

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## Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

## Policy History/Revision

| Date | Description of Change |
|---|---|
| 11/15/2024 | Reviewed. No changes. |
| 06/01/2024 | New medical document originating from SUR701.009. Coverage statement, which is unchanged states: Surgical closure of the left atrial appendage, including excision and epicardial clipping (i.e., AtriClip™) is considered not |

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|---|---|
| | medically necessary to reduce future stroke risk except when performed in conjunction with a Maze procedure for atrial fibrillation (AF). |