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Medical Policy Manual

Topic: Left-Atrial Appendage Closure Devices for Stroke Prevention in Atrial Fibrillation

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IMPORTANT REMINDER

Regence Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Percutaneous left-atrial appendage (LAA) closure devices have been developed as a nonpharmacologic alternative to anticoagulation for stroke prevention in atrial fibrillation. These devices are surgically implanted into the left atrium to occlude the left-atrial appendage, the region responsible for an estimated 90% of left-atrial thrombi. Low blood flow associated with atrial fibrillation raises the risk of thrombus and may lead to stroke in up to 5% of non-treated patients per year. Stroke associated with atrial fibrillation is primarily embolic in nature, tends to be more severe than the typical ischemic stroke, and causes higher rates of mortality and disability. Although anticoagulants (e.g. warfarin) are currently used to lower the risk of stroke in atrial fibrillation, their use is contraindicated in some patients, leaving few current treatment alternatives.

Regulatory Status

Several versions of LAA closure devices have been developed, but none have received FDA approval:

- The WATCHMAN® device, manufactured by Atritech Inc. While the U.S. Food and Drug Administration (FDA) advisory panel for this topic voted in favor of approval, the FDA did not grant final approval after concluding that further studies of efficacy and safety were necessary.
- The Cardioblate® closure device developed by Medtronic Corp. is currently being tested in clinical studies.

- The Amplatzer® septal closure device, manufactured by AGA Medical Corp. is FDA-approved for closure of atrial septal defects. This device has also been used as a LAA closure device; however, this use has not received FDA approval.
- The Amplatzer Amulet® device (St. Jude Medical,) has a CE approval in Europe for left atrial appendage closure, but is not currently approved in the U.S. for any indication.
- The Lariat® Loop Applicator device (SentreHEART, Inc,) is a suture delivery system that received 510(k) marketing clearance from the FDA in 2006. The intended use is to facilitate suture placement and knot tying in surgical applications where soft tissues are being approximated or ligated with a pre-tied polyester suture.

MEDICAL POLICY CRITERIA

The use of left-atrial appendage closure devices is considered **investigational** for all indications, including but not limited to the prevention of stroke in atrial fibrillation.

SCIENTIFIC EVIDENCE

The standard treatment for stroke prevention in atrial fibrillation is anticoagulation (warfarin or dabigatran), which has proven efficacy. In order to determine the safety and effectiveness of left-atrial appendage (LAA) closure devices for the prevention of stroke in atrial fibrillation, large, well-designed randomized controlled trials (RCTs) that compare this therapy to both sham and standard medical treatment (anticoagulation) are needed. Further, for chronic conditions such as atrial fibrillation, RCTs with long-term follow-up are necessary in order to determine durability of any beneficial treatment effects.

Literature Appraisal

The published evidence for LAA closure devices consists of a number of case series and two~~one~~ RCTs; one RCT compared LAA closure to warfarin anticoagulation and a subsequent RCT from the same trial reported on LAA closure devices in patients who were not candidates for warfarin. The evidence on each different device is reviewed separately, since the devices are not similar in design and may each have its own unique considerations.

<u>WATCHMAN device</u>

Randomized Controlled Trials

- The PROTECT-AF (Watchman Left Atrial Appendage System for Embolic Protection in Patients With Atrial Fibrillation) study was a randomized, unblinded trial that evaluated the noninferiority of an LAA closure device compared with warfarin for stroke prevention in atrial fibrillation.[1] The trial randomized 707 patients to the WATCHMAN® device or warfarin treatment in a 2:1 ratio. Mean follow-up was 18 months. The primary efficacy outcome compared the rate of stroke (ischemic or hemorrhagic), cardiovascular or unexplained death, or systemic embolism between the two groups and tested for noninferiority of the treatment group. There was also a primary safety outcome, which was a composite endpoint of excessive bleeding (intracranial or gastrointestinal [GI] bleeding) and procedure-related complications

(pericardial effusion, device embolization, or procedure-related stroke). Ischemic stroke occurred more frequently in the LAA closure group versus the warfarin group. The excess in adverse event rates for the LAA closure group were primarily the result of early adverse events associated with placement of the device. The most frequent type of complication related to LAA closure device placement was pericardial effusion requiring intervention, which occurred in 4.8% of patients (22/463).

- Longer term follow-up from the PROTECT-AF study was reported by Reddy et al. in 2012.[2] At a mean follow-up of 2.3 years, the results were similar to the initial report. The relative risk for the composite primary outcome in the Watchman group compared to anticoagulation was 0.71, and this met non-inferiority criteria with a confidence of >99%. Complications were more common in the Watchman group, with an estimated rate of 5.6%/year in the Watchman group compared to 3.6%/year in the warfarin group.
- As part of the PROTECT-AF trial, the same group of authors reported on LAA closure with the Watchman device in 150 patients with nonvalvular atrial fibrillation (AF) and $CHADS_2$ (congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, and prior stroke or transient ischemic attack) score ≥1, who were considered ineligible for warfarin treatment. Serious procedure- or device-related safety events occurred in 8.7% of patients (13 of 150 patients). All-cause stroke or systemic embolism occurred in 4 patients (2.3% per year): ischemic stroke in 3 patients (1.7% per year) and hemorrhagic stroke in 1 patient (0.6% per year).[3] Follow-up was limited to 14 months.
- Investigators administered the Short-Form 12 Health Survey at baseline and 12 months in a subset of 547 patients in the PROTECT-AF trial (361 device and 186 warfarin patients) to assess quality of life measures (QOL) between the 2 groups.[4] There was a significant improvement in QOL in patients randomized to device for total physical score, physical function, and in physical role limitation compared to control. Authors report that patients with nonvalvular AF at risk for stroke treated with left atrial appendage closure have favorable QOL changes at 12 months versus patients treated with warfarin.

In general, this study and subsequent substudies contribute to the body of knowledge concerning LAA closure devices and may be used to provide direction for future research. However, there was little evidence to support the safety of this device and the relatively short follow-up period (up to 18 months) may not be sufficient to evaluate durability of treatment effects.

Nonrandomized Studies

The published case series are primarily intended to establish safety of the device and do not consider efficacy.

- In 2011, Reddy and colleagues reported the adverse event rate from a registry of 460 patients who received the WATCHMAN® device.[5] Serious pericardial effusion occurred in 2.2% of patients, and there were no deaths or periprocedural strokes reported.
- Another report on the WATCHMAN device reported on the long-term risk of incomplete device closure on a group of 58 consecutive patients who had undergone device implantation.[6] Using a retrospective analysis, incomplete closure was noted in 16 (28%) of patients during implantation, 17 (29%) of patients at 45 days and 20 (35%) of patients at 12 months. Although the majority of gaps remained consistent or enlarged with time, in 8 patients, gaps closed or re-opened at successive time points. Stroke was the only clinical event measured; 1 patient with complete closure and 1 with incomplete closure had a stroke at 22 and 5 months, respectively. Statistical likelihood of incomplete closure was not reported, nor was risk of stroke.

Conclusion

Valid and reliable conclusions about the impact of LAA closure devices on health outcomes cannot be reached from these studies or others in the published literature due to several limitations, including but not limited to the lack of a control group.[7-12] Without an adequate control group it is not possible to account for the many types of bias that can affect study outcomes.

Lariat® device

The available evidence on the efficacy of the Lariat device consists of a number of small case series, most of which included less than 30 patients.[13-15] The largest case series was reported by Bartus et al. in 2012.[16] This study enrolled 89 patients with AF and either a contraindication to warfarin or previous warfarin failure. A total of 85/89 (96%) had successful left atrial ligation, and 81/89 (91%) had complete closure immediately. There were 3 access-related complications, 2 cases of severe pericarditis postoperatively, 1 late pericardial effusion, and 2 cases of unexplained sudden death. There were 2 late strokes, which the authors did not attribute to an embolic source. At one year of follow-up, complete closure was documented by echocardiography in 98% of available patients (n=65).

The following adverse effects with the Lariat device were reported in the studies described above:

- Unsuccessful placement
- Procedural complications
- Right ventricular perforation and tamponade
- Pleuro-peridicarditis
- Pericarditis developed within 30 days of the procedure.
- Periprocedural cerebrovascular accidents
- Stroke

Conclusion

The current studies above on the Lariat device reported high procedural success, but reported various complications that were included in all reviewed studies. Larger-scaled trials are needed to confirm the efficacy and safety of the Lariat device.

Amplatzer® Cardiac Plug device

The available evidence on use of the Amplatzer device for left atrial occlusion consists of a number of case series, most of which included less than 40 patients.[17-20] The largest series identified was by Nietlispach et al., which LAA occlusion was attempted in 152 patients from a single institution.[21] Amplatzer Cardaic Plugs were used in 120 patients and nondedicated devices were used in 32 patients. Short-term complications occurred in 9.8% (15/152). Longer-term adverse outcomes occurred in 7% of patients. In addition, a small study that included 86 patients diagnosed with non-valvular atrial fibrillation, the immediate results and short- to medium-term clinical follow-up of patients that underwent LAA closure with the Amplatzer device were described.[22] Authors reported 99% procedural success.

The following adverse effects with the Amplatzer Cardiac Plug device were reported in the studies described above:

- Cardiac tamponade
- Inappropriate plug size
- Coronary artery air embolism
- Device embolization
- Failed implantation
- Major bleeding
- Peripheral embolization
- Stroke
- TEE-attributed esophageal injury

Conclusion

All of these series reported high procedural success, but also reported various complications such as vascular complications, air embolism, esophageal injury, cardiac tamponade, and device embolization. Further large-scaled trials are needed to confirm the efficacy of this device.

Other devices

In 2010, Bayard and colleagues reported on 180 patients with nonrheumatic atrial fibrillation and a contraindication to warfarin and who were treated with the PLAATO (Percutaneous Left Atrial Appendage Transcatheter Occlusion) device.[23] Placement was successful in 90% of patients. Two patients died within 24 hours of the procedure (1.1%), and 6 patients had cardiac tamponade (3.3%), with 2 requiring surgical drainage. During a follow-up of 129 patient-years, there were 3 strokes, for a rate of 2.3% per year.

Clinical Practice Guidelines and Position Statements

There are no evidence-based clinical practice guidelines that recommend the use of the left-atrial appendage closure devices for the prevention of stroke in atrial fibrillation.

Summary

Currently, there are no left atrial appendage (LAA) closure devices that have approval from the US Food and Drug Administration (FDA) for use as an alternative to anticoagulation therapy for the treatment of atrial fibrillation. Currently, there are no devices that have FDA-approval for this indication in the U.S., but at least 3 different devices (Watchman®, Lariat®, and Amplatzer®) have been evaluated for this purpose. Overall, the evidence on LAA devices is limited in quantity and quality, and device safety has not been established. Given the lack of FDA approval and the limited data regarding impact on net health outcomes, use of left atrial appendage closure devices is considered investigational. Large, well-designed, randomized controlled trials with longer-term follow-up past two years are needed to determine the impact of LAA occlusion devices on net health outcomes.

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CROSS REFERENCES

None

CODES	NUMBER	DESCRIPTION
CPT	0281T	Percutaneous transcatheter closure of the left atrial appendage with implant, including fluoroscopy, transseptal puncture, catheter placement(s), left atrial angiography, left atrial appendage angiography, radiological supervision and interpretation
HCPCS	None	