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A Review Of Clinical Trials On LARIAT Device

Payam Safavi-Naeini, MD, Abdi Rasekh, MD, FACC

Department Of Cardiology (Drs. Abdi Rasekh And Safavi-Naeini), Texas Heart Insitute. Department Of Cardiology (Dr. Abdi Rasekh), Baylor College Of Medicine, Houston, Texas.

Abstract

The risk of embolic stroke is 5 times higher among patients with atrial fibrillation (AF) compared with those without AF. More than 90% of thrombi form in the left atrial appendage (LAA) in AF. The purpose of this review is to determine the efficacy and safety of the left atrial appendage (LAA) closure via a percutaneous LAA ligation approach, thus preventing a stroke among patients with AF and contraindication to oral anticoagulant therapy

Introduction

Atrial fibrillation (AF), an abnormal heart rhythm characterized by uncoordinated atrial activation due to multiple reentry circuits with consequent deterioration of atrial mechanical function, is the most common type of sustained arrhythmia.¹ In 2010, AF had an estimated prevalence of between 2.7 to 6.1 million, a frequency that is projected to increase to between 5.6 to 12 million by the year 2050.2 Its prevalence increases with age, rising from 0.1% in individuals younger than 50 years old, to 5.9% in those older than 65 years, and reaching to 10% after age 75.3,4,5 Stagnation of blood in upper chambers during AF increases the propensity of thrombus formation and makes a person 4-5 times more likely to have a ischemic stroke.² Patients with paroxysmal AF should be considered as having a stroke risk similar to individuals with persistent or permanent AF.6 Left atrial appendage (LAA) is the main site of clot formation, and more than 90% of thrombus are related to left atrial appendage dysfunction.7 AF is associated with increased risk of stroke severity, and patients with AF-related stroke have twofold the risk of mortality and threefold the risk of recurrent stroke within 1 year compared with patients without AF.8 The annual rate of ischemic stroke in patients with AF is approximately 5%, which is responsible for about 15% of strokes in the United States.9 AF-related stroke is a substantial economic burden and costs Medicare about \$8 billion annually.¹⁰ Oral anticoagulation (OAC), with warfarin or new alternative antithrombotic agents (e.g.: apixaban, dabigatran, and rivaroxaban), is the current standard therapy for stroke prevention in patients with AF.11

Disclosures: None.

Corresponding Author: Dr.Abdi Rasekh, MD, FACC Department Of Cardiology Texas Heart Insitute, Texas. Nevertheless, many patients (up to 40%) with AF do not receive appropriate preventive therapy for stroke.^{12,13} The drug–drug and drug–food interactions, variable drug metabolism and the difficulty of keeping patients in therapeutic range, the hardship of need for regular monitoring, and increasing risk of bleeding are serious concerns in using OAC. When using OAC, the rate of major bleeding is around 3% per year, and there is no major difference between warfarin or new OAC.^{14,15} In patients with AF at high risk of stroke, who either had contraindications to OAC therapy or previous failure of OAC therapy, utilizing a percutaneous LAA closure device (LARIAT snare device; SentreHEART, Inc., Palo Alto, California) is an alternative approach in order to prevent stroke.¹⁶

Percutaneous Suture Ligation For LAA Closure

LARIAT Suture Delivery Device (SentreHEART, Redwood City, California) is a new approach to LAA exclusion in patients who are high risk for stroke and contraindicated to or intolerant of standard oral anticoagulation therapy. The LARIAT procedure is performed under general anesthesia and the device consists of 3 components: 1) a 20-mm compliant balloon catheter (EndoCATH®), 2) 0.025" and 0.035" opposite-pole magnet-tipped guide wires (FindrWIRZ), and 3) a 12F suture delivery device.¹⁶

A 0.025-inch magnet-tipped guide wire (FindrWIRZ; SentreHEART, Inc.), is placed in the apex of the LAA through the transseptal sheath. A 0.035-inch magnet-tipped guide wire is then directed to the LAA via the pericardial space through the epicardial guide cannula (SentreHEART, Inc.) and is manipulated until its magnetic tip binds to the 0.025-inch magnet-tipped endocardial guide wire. After connecting the two magnetic wires, the LARIAT snare is advanced over the epicardial magnet-tipped wire and placed on the proximal portion of the LAA. The LARIAT suture delivery device places and tightens a loop stich around the base of the LAA with a pre-tied suture loop. The suture is released and tightened after confirmation of complete closure by the LAA Doppler (flow less than 5 mm on cross section) and the LARIAT snare is removed from the pericardial space. The surgical suture permanently seals the LAA off from the rest of the heart and the excluded LAAs will shrink thereafter.¹⁶

Selection Criteria For Lariat Procedure Among Patients With Atrial Fibrillation

The Inclusion Criteria Included:17

1) CHADS2 score \geq 2 or CHADS2VASc score \geq 3,

2) Contraindicated to or intolerant of standard oral anticoagulation (OAC) therapy (due to history of internal or external bleeding, or high risk for bleeding),

3) Failure of OAC (embolic event despite OAC),

4) Intolerance or difficulty in using OAC.

The Exclusion Criteria Included:11

1) History of cardiac surgery,

2) Myocardial infarction within the previous 3 months,

3) Embolic events within the past 30 days,

4) New York Heart Association class IV heart failure symptoms,

5) History of thoracic radiation therapy,

6) A superior oriented LAA or one larger than 40 mm.

Procedure Outcomes

Our initial experience at Texas Heart Institute of LAA exclusion by LARIAT in a cohort of patients with high risk of embolic events and contraindicated to or intolerant of standard oral anticoagulation demonstrated > 90% acute success rate. Transesophageal echocardiography (TEE) at 2 to 3 months follow-up showed 100% LAA occlusion.

In addition to our experiment, two other studies have been published.^{16, 18,19} The safety and efficacy trends of the LARIAT continue to be maintained in these two independent studies. Both patient groups were at high risk of stroke and contraindicated to OAC therapy. This appears to be the real-world compatibility of the LARIAT in treating patients with limited options for protection. (Table I)

In these studies, there were no device related complications using the LARIAT. Access related complications tended to be related to pericardial access, and the majority of them were not major and selfresolved during or shortly after the procedure. Furthermore, in these studies, only three deaths occurred during the follow-up, which were unrelated to the procedure.

Meanwhile, preliminary data analysis showed promising results at our center's one-year follow-up. Among 40 patients, at 3 months follow-up with TEE, we observed 2 leaks (one <1 mm and the other around 2-3 mm) and one blood clot, which resolved by OAC therapy. No CVA detected at 12 months follow-up with Questionnaire for Verifying Stroke-Free Status (QVSFS)²⁰ and only one patient had stroke at 18 months after the procedure with no evidence of blood clot in afterward follow-up TEE. We are submitting a multi-centric follow-up study, which will provide us with profound insight into the long-term effectiveness of the LARIAT procedure in preventing strokes.

Proposed Multi-Centric Cohort Studies

Sentreheart Stroke Study

The purpose of this prospective, multi-center, randomized (1:1) trial study is to assess the effectiveness of the LARIAT Suture Delivery Device to reduce the risk of stroke and thromboembolic com
 Table 1:
 Published procedure outcomes: Acute success rate, Complications and efficacy to prevent stroke.

	Randall Lee, et al (19)	Rasekh , et al(16)	Pershad, et al (18)
Patients population	89	21	27
Intent-to-Treat	85 (96%)	20 (95%)	25 (93%)
Procedural Closure	82 (95%)	19 (95%)	25 (100%)
>90day Closure w TEE	81 (97%)	17 (94%)	22 (100%)
Mean CHADS2 Score	1.9+0.95	3.2+1.2	3.5+1.4
Patients follow-up	One year	An average of 352 ±143 days (range 50 to 600)	An average of 4.0±3.4 months (range 0.1-12.7 months)
Device Related Complications	0	0	0
Access Related Complications	3 (3%)	1(5%)	1 (3.7%)
All Death	2 (2%)	1(5%)	0
All Stroke	2 (2%)	0	1 (3.7%)
Major Bleeding	0	0	1 (3.7%)
Pericardial/Pleural Effusion	1(1%)	3 (15%)	2 (7.4%)
Device Replacement	0	0	0

plications in patients with non-valvular atrial fibrillation who are at risk for embolic events and are unable to use standard oral anticoagulation therapy.

Primary Efficacy Outcome: To assess time to the composite endpoint (first event of ischemic/hemorrhagic stroke or systemic embolism) in participants randomized to the LAA exclusion procedure using the LARIAT Suture Delivery Device compared to participants in the Control Group.

Primary Safety Outcome: To assess the incidence of major bleeding events in participants randomized to the LAA exclusion procedure using the LARIAT Suture Delivery Device compared to participants in the Control Group.

Sentreheart Feasibility IDE (Investigational Device Exemptions).

This is a feasibility study to demonstrate the technical ability of the LARIAT device to electrically isolate left atrial appendage as an initial step in the treatment of patients with persistent or longstanding persistent atrial fibrillation.

Technical Success: The ability of the LARIAT device to be successfully placed around the left atrial appendage to achieve electrical isolation defined as a reduction in LAA voltage amplitude of at least 50% of baseline voltage.

Procedural Success: The ability to achieve technical success without any device related serious adverse events through 30 days post

Af Success: AF Burden shall be evaluated at 1, 3, 6, 12 months post Pulmonary Vein Isolation (PVI) procedure.

Is It Possible To Increase The Efficacy Rates Of AF Ablation With Concomitant LAA Exclusion?

Two studies examine the possibility of this hypothesis. In one study, Han et al. reported that, there was a significant reduction in the mean LAA voltage after successful LAA ligation procedure (64 out of 68 patients). Unipolar and bipolar pre-ligation voltage reported 1.1 \pm 0.53 mV and 4.7 \pm 2.83 mV respectively comparing to unipolar (0.3 \pm 0.38 mV) and bipolar (0.6 \pm 0.27 mV) post-ligation voltage.²¹

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The other study showed that the atrial arrhythmia burden decreased from 81% to 47% (p<0.01) at 3 months follow-up among 18 patients with AF and a cardiac device, who had the LARIAT procedure.²² A new multi-center FDA approved clinical trial (AMAZE Trial) was just initiated to evaluate the possible role of LAA closure by lariat to increase the success rate of AF ablation in patients with persistent or longstanding persistent AF.

Discussion

Prevention of atrial fibrillation-related stroke has a great role in AF treatment.

The promising acute success rate of the LAA closure with LAR-IAT (> 90%), and low incidence of embolic events in high risk patients following the LAA ligation, suggests that LAA ligation with LARIAT device may be a protective option in preventing strokes in patients who have contraindications to oral anticoagulation.

The results of aforementioned proposed trials will extend our knowledge about the efficacy of LARIAT to prevent strokes or the possible role of concurrent LARIAT to increase the success rate of AF ablation.

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