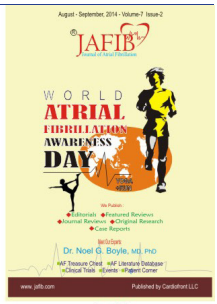
JAFIB
Original Research
Journal of Atrial Fibrillation
www. jafib.com



Retrospective Evaluation Of Novel Percutaneous Left Atrial Appendage Ligation Using The Lariat Suturing Device: Single Center Initial Experience

Soidjon Khodjaev MD, Duong Le, MD, MSc, Wei Rao MD, Remo Morelli MD, FACC

Department of Cardiovascular Medicine. St. Mary's Medical Center San Francisco, CA, USA. Soidjon D. Khodjaev MD. Department of Cardiovascular Medicine. St. Mary's Medical Center. San Francisco, California. USA and Department of Cardiology at SFVAMC/University of California, San Francisco, CA, USA. Duong L. Le MD, MS Department of Cardiovascular Medicine. St. Mary's Medical Center. San Francisco, CA, USA. Wei Rao MD. Department of Cardiovascular Medicine. St. Mary's Medical Center. San Francisco, CA, USA. Remo L. Morelli MD, FACC. Department of Cardiovascular Medicine. St. Mary's Medical Center. San Francisco, CA, USA.

Abstract

Background: The left atrial appendage (LAA) is the source of considerable thromboemboli responsible for embolic strokes in patients with atrial fibrillation (AF). The LARIAT™ suturing device has been used to ligate the LAA and negate the use of systemic anticoagulation. However, its efficacy and stroke outcome is still unknown.

Methods: We retrospectively evaluated the clinical status and risk of occurrence of systemic emobolic events, strokes, transient ischemic attacks, and procedure related complications in patients after LAA ligation using the LARIAT™ device.

Results: Permanent suture was successfully delivered in 21 patients. Mean follow up time was 17.2+-3.3 months. The average HAS-BLED score was 3.3+/-1.1. Only 1 patient developed clinical symptoms of stroke 7 days post procedure. One patient had uncomplicated perioperative bleeding not requiring blood transfusion. One patient developed transient ECG changes of ischemia during mapping for ablation following the LAA ligation and subsequently, underwent bypass surgery. Three patient developed post-procedural pericarditis and were medically managed. Three patients died from non-LAA ligation related conditions including congestive heart failure, lung cancer, and severe coronary disease. We observed a 32% and 30% reduction in the annual risk of stroke when compared to the expected risk of stroke based on the $CHADS_2$ and CHA_2DS_2-VASc score respectively.

Conclusion: LAA ligation using the LARIAT™ suturing device is clinically feasible in carefully selected patients. This study has the longest follow up period to date, however further studies are required to determine the efficacy of stroke reduction and long-term clinical outcomes.

Introduction

Atrial Fibrillation (AF) is the most common arrhythmia treated in clinical practice and accounts for 15-20% of all strokes in the United States.[1,2] Embolic stroke is the most devastating and fearful complication of AF. These detrimental effects were explained by its two-fold increase in all-cause mortality.[3,4] Based on autopsy and echocardiography studies, the left atrial appendage (LAA) is considered to be the nidus of greater than 90% of thromboemboli in AF patients.[5,6,7]

There have been great interests in eliminating the LAA as a source of emboli through a catheter based approach. An epicardial-deployed percutaneous LAA ligation device using the LARIAT™ (Sentre-Heart, Redwood City, CA, USA) has been described in the literature to exclude the LAA.[8,9] Although LAA ligation using the LARIAT™ suturing device obviates the need for oral anticoagulation therapy, there are limited studies that evaluate the occurrence of thromboembolism and long-term clinical outcomes utilizing the LARIAT™ suture device. In this retrospective study, we seek to evaluate the clinical status and the occurrence of thromboembolism in patients who have undergone LAA ligation with the LARIAT™ device.

Materials And Methods

With approval from the St. Mary's Medical Center Institutional Review Board we conducted a retrospective data analysis on patients who underwent LAA ligation using the LARIAT™ suture device from February 2011 to November 2012 at St. Mary's Medical Center San Francisco, CA, USA. A total of 22 patients were identified and evaluated. The follow up period was determined from the day of the procedure to April 2013. Data collection included paper based charts, electronic medical records, direct phone interview with patients, primary care provider, and specialists.

Inclusion criterion was an attempt to perform LAA ligation with the LARIAT™ suture device from February 2011 to November

Key Words:

LARIAT Suturing Device, Laa Ligation, Stroke Prophylaxis.

Disclosures:
None.

Corresponding Author:
Soidjon D. Khodjaev MD,
USA and Department of Cardiology at SFVAMC/University of California,
San Francisco, CA, USA.

Table 1: Baseline characteristics

PATIENTS	GENDER	AGE (YEARS)	$CHADS_2$ SCORE	CHA_2DS_2-VASC SCORE	HAS-BLED SCORE	FOLLOW UP (MONTHS)
1	M	73	3	4	5	25
2	F	80	3	5	4	24/ Deceased
3	F	84	3	5	5	23
4	M	62	1	2	2	21
5	F	58	2	3	3	12
6	F	72	4	6	4	Lost to follow up
7	M	82	2	3	4	12
8	M	57	3	3	1	25
9	M	63	3	5	3	24/ Deceased
10	M	55	2	3	3	14
11	F	68	2	4	2	15
12	F	60	4	5	3	11
13	M	55	2	4	2	5
14	M	85	3	4	3	Unsuccessful attempt/ Deceased
15	F	89	2	4	3	26
16	F	87	2	4	3	5
17	F	87	2	5	3	6
18	F	71	3	5	4	21
19	M	80	3	5	4	24
20	F	70	1	3	3	Lost to follow up
21	M	81	4	5	5	8
Ave +/- SD	_	73 +/- 4.7	2.6 +/- 0.87	4.1 +/- 1.1	3.3 +/- 1.1	17.2 +/- 7.8

2012 at St. Mary's Medical Center, San Francisco and provide informed consent. Exclusion criterion included all patients who did not undergo an attempt to perform LAA ligation.

Outcomes

The primary outcomes were the occurrence of systemic thromboembolic events or TIA within the time observed. The secondary outcomes included successful peri-operative closure of the LAA (defined as <5-mm residual leak by perioperative TEE color Doppler evaluation), the occurrence of peri-procedural and post-procedural complications such as life-threatening hemorrhagic events (ex: requiring surgery or blood transfusion), pericardial effusions, pericarditis, cardiac tamponade, myocardial infarction, stroke, and all-cause mortality.

Procedure

The LARIAT™ device and accessories consists of a 15-mm compliant occlusion balloon catheter (EndoCATH™), a 0.025-inch and 0.035-inch magnet-tipped guidewires (FindrWIRZ™), and a 12-F suture delivery device (LARIAT™). The steps and procedures are detailed in previous studies.[8,9] Patients who had evidence of thrombi in the LAA, a clinical history of open-heart surgery, severe pericarditis, pre-procedure CT angiogram demonstrating the following: LAA width > 40mm, superiorly oriented LAA with the LAA apex directed behind the pulmonary vascular trunk, bi-lobed LAA or multi-lobed LAA in which lobes are oriented in different angles, and a posteriorly rotated heart were not considered as a candidate for the procedure.[10]

Statistical Methods

All categorical and continuous variables are summarized by mean, standard deviation, and range. Estimates of occurrence of events are expressed as percentage. $CHADS_2$, CHA_2DS_2-VASc, and HAS-BLED scores were individually scored and averaged to calculate the expected risk of stroke or bleeding risk. The observed risk of stroke was determined by rate of stroke or TIA per patient-time as expressed by percentage.

Results

Twenty-two patients underwent attempted LAA ligation and permanent suture was successfully delivered in 21 (95%) patients. Table 1 shows the baseline characteristics of the patients who underwent LAA ligation. A procedure was aborted due to pericardial adhesions from previously unrecognized pericarditis. Eighteen patients (86%) had paroxysmal AF, 1 patient had permanent AF (0.5%), and 2 patients had persistent AF (9.5%). One patient refused to participate in the study after undergoing the procedure and 2 patients were lost to follow up.

The majority of our patient population had a high $CHADS_2$ score and one-third of the patients had a prior stroke/TIA (see table 2 for details). Six (29%) patients had history of GI bleed, 8 (38%) refused warfarin therapy due to fear of bleeding complications and/or therapy regimen discomfort, and 4 patients (19%) did not tolerate warfarin therapy due to GI discomfort (see table 3 for details).

Our patient population also had a high risk for bleeding with an average HAS-BLED score of 3.3+/- 1.1. All patients were on oral anticoagulation prior to the procedure. A large majority of the patients (76%) were discharged with no oral anticoagulation therapy (see table 4 for details). One patient was discharged with dabigatran which was discontinued after the patient underwent pulmonary vein isolation and ablation, 1 patient remained on dabigatran due to prior evidence of a small thrombus in the LAA which was discontinued after sufficient duration of therapy, 1 patient was discharged with aspirin and rivaroxaban until the patient underwent pulmonary vein isolation and ablation, 1 patient was discharged with warfarin for upper extremity deep vein thrombosis and then later switched to dabigatran after suffering a stroke that was presumed as a lacunar infarction but could not completely exclude an embolic stoke, and 1 patient was discharged on warfarin which was discontinued after pulmonary vein isolation and ablation.

Primary Outcome

Only 1 patient had clinical symptoms of stroke 7 days after the procedure. The stroke was thought to be due to a lacunar infarction due to uncontrolled hypertension. The patient underwent rehabilitation therapy and was discharged home at near baseline functional status. There were no other thromboembolic events seen in patients included in this study.

Secondary Outcome

Twenty patients (95%) who underwent an attempted procedure had successful peri-operative closure of the LAA. One patient experienced non-life threatening peri-procedural pericardial bleeding that did not require blood transfusion. One patient developed transient ST-segment elevation during mapping for planned AF ablation once LAA ligation was completed. Mapping was aborted and coronary angiogram revealed two vessel disease. The patient subsequently underwent two vessel coronary artery bypass grafting. No patients had evidence of significant pericardial effusion requiring prolonged

Table 2: $CHADS_2$ and CHA_2DS_2-VASc characteristics

$CHADS_2$	Total (N = 21)
1	2 (9.5%)
≥ 2	19 (90.5%)
Average Score	2.6 +/- 0.87
CHA_2DS_2-VASc	**Total (N = 21)**
0-1	0
≥ 2	21 (100%)
Average Score	4.1 +/- 1.1

C-Congestive Heart Failure; H-Hypertension; A-Age; D-Diabetes Mellitus; S-Stroke or Transient ischemic attack or Systemic embolism; VA-Vascular disease; Sc-Sex Category

pericardial drainage (<48 hours), and cardiac tamponade.

Three (16%) patients developed clinical pericarditis with pleuritic chest pain that was managed with colchicine and NSAIDs. Three (16%) patients died during the follow up period from non-procedure related conditions: 1 patient died from metastatic small cell carcinoma of the lung, 1 patient died from severe coronary artery disease and heart failure, and 1 patient who was attempted but did not undergo the complete procedure died from multiple co-morbidities, including coronary artery disease, congestive heart failure, and dementia.

Discussion

The cornerstone for the management of chronic non-valvular AF is stroke reduction with oral anticoagulation. However, poor compliance and bleeding side effects have severely limited their use which creates a therapeutic dilemma. As much as 20% of AF patients are not receiving oral anticoagulation due to contraindications and less than half of AF patients are on oral anticoagulation due to either physician reluctance or patient non-compliance.[11,12] This dilemma is the impetus for procedures that can lower stroke risk and bleeding without oral anticoagulation.

In our study population, our patients were at a high risk for stroke and bleeding. The majority of the patients had a $CHADS_2$ score ≥ 2 (90%). This confers to an expected annual stroke risk of 5.4% compared to a 5.2% expected stroke risk based on the CHA_2DS_2-VASc score. The rate of stroke per 100 patient-year was 3.6% which is a 32% reduction in annual stroke risk based on $CHADS_2$ score and 30% reduction in annual stroke risk based on the CHA_2DS_2-VASc score (Figure 1). Our study population had an appreciable high bleeding risk with an average HAS-BLED score of 3.3+/-1.1. This

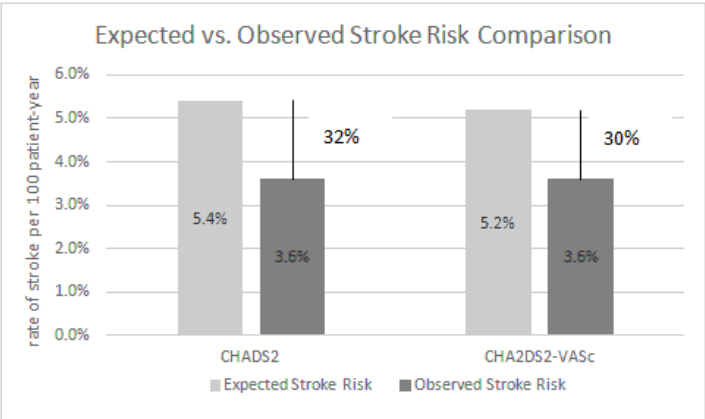


Figure 1: Annual stroke risk based on the CHA_2DS_2-VASc score

Table 3: Indications for left atrial appendage ligation

Indications	Total (N = 21)
Bleeding of any type	8 (38%)
Intracranial hemorrhage	3 (14%)
Non-intracranial hemorrhage	6 (29%)
High fall risk	1 (5%)
Intolerance to anticoagulation	4 (19%)
Occurrence of stroke on therapeutic anticoagulation	1 (5%)
Personal preference to stop anticoagulation	8 (38%)

confers a 6.7% annual bleeding risk. Of note, all patients were on anticoagulation prior to the procedure and the majority of the patients (76%) remained off of oral anticoagulation post-procedure. This is highly advantageous given a population with a high bleeding risk.

There are limited studies evaluating the long-term stroke outcomes in patients who have undergone LAA ligation using the LARIAT™ suture device. See table 5 for comparison details. In a small case series by Massumi et al, they evaluated 21 patients who were similar to our patient population in regards to risk for stroke and bleeding (average $CHADS_2$ score 3.2 +/- 1.2, mean HAS-BLED score 3.5 +/- 1.0).[13] All patients underwent successful LAA ligation.[13] There were no strokes observed during an average of 352 +/- 143 days of follow-up.[13] In another series of 27 high risk patients ($CHADS_2$ score of 3.5 +/- 1.4 and HAS-BLED score of 4.6 +/- 0.9), Stone et al demonstrated successful LAA ligation in 25 patients.[14] They observed 1 stroke after 33 days of follow-up.[14] The stroke was contributed to atheroma in the aortic arch.[14] These results are consistent with our observation of 1 stroke over an average of 460 days. However if the clinical observation of stroke is adjudicated to a non-embolic event then the occurrence of embolic stroke is negligible. Nonetheless, albeit small sample size, our findings are consistent with previous case series and confirms the longest follow up period up to date. Also, it should be noted that there is no current consensus on post procedure anticoagulation and/or antiplatelet therapy which may limit efficacy of stroke outcome.

The advantages of this procedure include the negligible need to deploy a foreign occlusion device to accommodate various appendiceal ostium morphologies, and potentially the need for short term anticoagulation post device implantation as demonstrated by other occlusion devices.[15] The disadvantages of this procedure are primarily related to the challenges in achieving access to the pericardium and LAA anatomy. Minor adverse effects include pericarditis, pericardial effusions, and bleeding; while severe complications include: right ventricular perforation, cardiac tamponade, and potential damage to the epicardial vessels.[12] However with improved imaging modalities such as combined 2-D and real time 3-D TEE, better characterization of the appendage and intraprocedural visualization of wires, balloons, and catheters may lead to improved outcomes.[16] In our

Table 4: Post-procedure anticoagulation/antiplatelet characteristics

Type of anticoagulation/antiplatelet post-procedure	Total (N = 19)
None	8 (42%)
Aspirin only	7 (37%)
Dabigatran	2 (11%)
Aspirin and Rivaroxaban	1 (5%)
Warfarin	1 (5%)

Table 5: Comparison between studies availables

Study	N (Successful Closure/Attempted)	Follow-up In Months	Ave $CHADS_2$ Score	Ave CHA_2DS_2-Vasc Score	Ave HASBLED Score	Expected Embolism Rate	Observed Embolism Rate
Massumi et al.[13]	20/21	Ave 11.7 +/- 4.8*	3.2 +/- 1.2	4.8 +/- 1.3	3.5 +/- 1.0	4-7%	0% (0/20) at observed follow up
Stone et al.[14]	25/27	Ave 4.0 +/- 3.4	3.5 +/- 1.4	5.1 +/- 1.5	4.6 +/- 0.9	9-12%	4% (1/25) at 33 days follow up
Khodjaev et al.	21/22	Ave 17.2 +/- 7.8	2.6 +/- 0.87	4.4 +/- 1.1	3.3 +/- 1.1	3-7%	5% (1/21) at 7 days follow

*Follow up was converted from days to months

patient population, pericarditis was a common complication (16%) that was treated medically with NSAIDs and oral colchicine. No patients received intra-pericardial steroids or the need for surgery. There were no cases of right ventricular perforation, cardiac tamponade, or life-threatening bleeding.

There are obvious limitations to our study. The retrospective nature of study, small sample size, non-randomization, and no comparison group seriously limits an accurate assessment between the procedure and its true effect on stroke reduction. Therefore, no conclusions can be made about the efficacy of stroke prevention compared to chronic oral anticoagulation therapy or other LAA exclusion techniques.

Conclusion:

With careful patient selection and preoperative evaluation, LAA ligation using the LARIAT™ suturing device is clinically feasible. The overall challenges of this technique and risk serious complications can be reduced with increased operator experience.[13] Although our study is an observational, retrospective, and uncontrolled study with similar outcomes compared to other case series, further studies are required to determine the efficacy of this technique in regards to stroke reduction and long-term clinical outcomes. Moreover, this study recapitulates the need for studies that compare this technique to other oral anticoagulation therapy.

References:

1. Go AS, Hylek EM, Philips KA, Chang Y, Henault LE, Selby JV, Singer DE. Prevalence of diagnosed atrial fibrillation in adults: national implications for rhythm management and stroke prevention: the Anticoagulation and Risk Factors in Atrial Fibrillation (ATRIA) Study. JAMA 2001; 285:2370-2375.
2. Miyasaka Y, Barnes ME, Gersh BJ, Cha SS, Bailey KR, Abhayaratna WP, Seward JB, Tsang TS. Secular trends in incidence of atrial fibrillation in Olmsted County, Minnesota 1980 to 2000, and implications on the projections for further prevalence. Circulation 2006;114:119-125.
3. Loyd-Jones D, Adams R, Carnethon M, De Simone G, Ferguson T. B, Flegal K, Ford E, Furie K, Go A, Greenlund K, Haase N, Hailpern S, Ho M, Howard V, Kissela B, Kittner S, Lackland D, Lisabeth L, Marelli A, McDermott M, Meigs J, Mozaffarian D, Nichol G, O'Donnell C, Roger V, Rosamond W, Sacco R, Sorlie P, Stafford R, Steinberger J, Thom T, Wasserthiel-Smoller S, Wong N, Wylie-Rosett J, Hong Y. : Heart disease and stroke statistics -2009 updates: A report from the AHA Statistics Committee and Stroke Statistics Subcommittee. Circulation 119:e21, 2009.
4. Henrik Stig Jørgensen, MD; Hirofumi Nakayama, MD, PhD; Jakob Reith, MD; Hans Otto Raaschou, MD; Tom Skyhøj Olsen, MD, Ph. Acute Stroke with Atrial Fibrillation. The Copenhagen Stroke Study. Stroke.1996; 27: 1765-1769
5. Blackshear Jl, Odell JA, Appendage obliteration to reduce stroke in cardiac surgical patients with atrial fibrillation. Ann. Thorac. Surg. 1996; 61:755-59.
6. Al-Saady NM, Obel OA, Camm AJ. Left atrial appendage: structure, function, and role in thromboembolism. Heart 1999; 82:547-555.
7. Alberg H. Atrial fibrillation: a study of atrial thrombus and systemic embolism in a necropsy material. Acta Med Scand 1969; 185:373-79.
8. Lee RJ, Bartus K, Yakubov SJ. Catheter-Based Left Atrial Appendage (LAA) Ligation for the Prevention of Embolic Events Arising From the LAA. Initial Experience in a Canine Model. Circ Cardiovasc Interv. 2010; 3:224-229.
9. Morelli R, Khodjaev S. Percutaneous Left Atrial Appendage Closure Ligation and Exclusion as an Alternative Stroke Prevention in Patients with Nonvalvular Atrial Fibrillation. EP Lab Dig 2012; 20-22.
10. Koneru JN, Badhwar N, Ellenbogen KA, Lee RJ. LAA ligation using the LARIAT suture delivery device: tips and tricks for a successful procedure. Heart Rhythm. 2014; 21:S1547-5271.
11. Stafford RS, Singer DE. Recent national patters of warfarin use in atrial fibrillation. Circulation 1998; 97:1231-1233.
12. Gottlieb LK, Salem-Schatz S. Anticoagulation in atrial fibrillation. Does efficacy in clinical trials translate into effectiveness in practice? Arch Intern Med 1004; 154(17): 1945-1953.
13. Massumi A, Chelu MG, Nazeri A, May SA, Afshar-Kharaghan H, Saeed M, Razavi M, Rasekh A. 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 2013; 111:869-873.
14. 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. 2013 Jun 13. Doi:10.10002/ccd.25065. [Epub ahead of print].
15. Holmes DR, Reddy VY, Turi ZG, Doshi SK, Sievert H, Buchbinder M, Mullin CM, Sick P. Percutaneous closure of the left atrial appendage versus warfarin therapy for prevention of stroke in patients with atrial fibrillation: a randomized non-inferiority trial. Lancet 2009; 374:534-542.
16. Laura DM, Chinitz LA, Aizer A, Holmes DS, Benenstein R, Freedberg RS, Kim EE, Saric M. The Role of Multimodality Imaging in Percutaneous Left Atrial Appendage Suture Ligation with the LARIAT Device. J Am Soc Echocardiogr 2014; 27(7): 699-708.