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PROTOCOL

STUDY TITLE: Left Atrial Appendage Closure with SentreHeart Lariat® Device

SITE LOCATION: The Heart Hospital Baylor Plano
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ADDITIONAL SITES: Baylor Jack and Jane Hamilton Heart and Vascular Hospital
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1. BACKGROUND & STUDY RATIONALE

Left atrial appendage and stroke

Stroke, particularly cardioembolic stroke, is a frequent and serious complication of atrial fibrillation. Previous reports have shown that the left atrial appendage (LAA) is the source of embolus in the majority of patients who suffer this complication.

Traditionally, oral anticoagulant medications (OAC) have been used to reduce the risk of embolic stroke in patients with atrial fibrillation. Warfarin has been the most frequently used agent in this regard. Recently dabigatran, rivaroxaban, and apixaban have been introduced for the same purpose. These novel agents have potential advantages over warfarin; they are less susceptible to dietary and drug-drug interactions. Due to their mechanism of action, routine INR testing is not necessary. For these reasons, their use is increasing, and many physicians report increased compliance with anticoagulation with the newer regimens. However, there is a significant patient population who continue to be at elevated bleeding risk with the use of any OAC. Patients with clinically significant bleeding, intracranial hemorrhage, and patients with a prohibitively high risk of falls often do not receive OAC therapy, and remain at elevated risk for stroke.

Left atrial appendage management

There are at the present three methods of addressing management of the LAA aside from oral anticoagulant therapy: Surgical excision, external ligation of the appendage, and internal occlusion of the left atrial appendage.

Surgical excision is generally performed during a concomitant cardiac procedure. The proximal portion of the appendage is closed with sutures or staples, and the trabeculated portion is removed. This has been shown to reduce risk of stroke after cardiac surgery. Surgeons note that this can result in significant bleeding, and other alternatives have recently been employed.

Internal occlusion is accomplished via a transseptal approach. The Watchman® device (Boston Scientific, Inc.) has completed its second controlled trial. The results of the PROTECT-AF trial were presented at the Heart Rhythm Society Scientific Sessions in Denver, CO on May 9, 2013, and seemed to show non-inferiority, and in some endpoints, superiority to, medical therapy with warfarin. The Amplatzer Cardiac Plug® trial was discontinued by the sponsor, and no public announcement has been made regarding restarting the trial. For both of these devices, OAC therapy is required for at least 45 days post-procedure. OAC therapy is required for a greater period of time if LAA closure is incomplete.

Two devices have been used in multiple centers in the US for ligation of the LAA, the AtriClip® (AtriCure, Inc) and the SentreHeart Lariat® (SentreHeart, Inc). The AtriClip® is a surgical device approved for LAA closure *in patients undergoing other cardiac procedures*. Deployment of the AtriClip® has not received an FDA indication as a stand-alone procedure. The Lariat® device is approved for soft tissue ligation, without a specific indication for LAA closure.

2. STUDY OBJECTIVES

Objectives

1. The primary aim is to assess the outcome of patients undergoing left atrial appendage ligation or closure with the SentreHeart Lariat® device as a stand-alone procedure at the participating centers
2. Secondary aims include assessment of adverse events and successful LAA closure rates

Hypothesis

Closure of the left atrial appendage with the SentreHeart Lariat® is reasonable alternative to reduce the risk of stroke in patients with an elevated bleeding risk with the use of any OAC and in whom this risk is prohibitive.

3. STUDY DESIGN

The study is a multi-center, prospective outcomes registry. The study cohort will comprise all consecutive patients who undergo lone left atrial appendage closure using the SentreHeart Lariat® at the investigational centers and should consist of up to 50 patients. Patients will undergo follow-up visits at 7 days, 90 days, and 180 days post procedure.

4. STUDY POPULATION

The study cohort will consist of up to 50 patients who are candidates for LAA closure in whom oral anticoagulation is contraindicated.

4.1 Inclusion Criteria

- Patients aged ≥18 years
- Patients able and willing to provide informed consent
- Documentation of atrial fibrillation or atrial flutter
- Clinical decision by the subject's physician that the patient is at risk for embolic stroke, and OAC is contraindicated (using the assessment outlined in Table 1)
- HAS-BLED score $\geq$ 3
- $CHADS_2$-VASC score $\geq$3, OR $CHADS_2$-VASC of 2 if physician provides justification for procedure
- Anatomy favorable for deployment of the SentreHeart Lariat®

4.2 Exclusion Criteria

- Medically unable to provide informed consent
- Previous cardiothoracic surgery
- Patient is a candidate for catheter or surgical ablation
- Need for concomitant cardiac surgery procedure
- Thrombus in the left atrial appendage or left atrium
- Pregnancy

4.3 Inclusion of special, vulnerable or high risk populations

4.3.1 Elderly

Atrial fibrillation and atrial flutter are most common in the aging population and would account for the inclusion of this population. Ample time will be allotted to assure that this population has the opportunity to carefully read the consent, share this information with family members, and discuss the objective of the study along with any risks/benefits that may be expected. Subjects will have all of their questions answered before signing the consent and taking part in the study.

5. ENROLLMENT & STUDY PROCEDURES

Subjects evaluated for left atrial appendage closure will be screened for inclusion and consented prior to their procedure. During clinical evaluation of the patient, the physician investigator will assess those items described in Table 1. If the anatomy is favorable for placement of the Lariat® device, the procedure will be performed at one of the participating centers. If anatomy is not favorable, the patient will be excluded from the study and managed using best care practices by his or her physician. Please note, at The Heart Hospital Baylor Plano, the Lariat device is only available to patients participating in the study.

Subjects consented will be tracked by the study team and will be considered enrolled in this study at the time of the start of their left atrial appendage closure procedure. All subjects that are consented who do not undergo left atrial appendage closure with SentreHeart Lariat® will be considered screen failures. Any patients that have a failed attempt at left atrial appendage closure with SentreHeart Lariat® will be tracked through their index hospitalization for safety; their study follow up will be complete at the time of discharge.

The invasive procedure for placement of the study devices will proceed according to standard interventional techniques, as already in place at the participating centers. Patients undergoing the Lariat® procedure will be administered colchicine 0.6 mg po twice daily for a minimum of three days preoperatively, and 30 days postoperatively. (This dose may be adjusted for renal function or intolerance).

5.1 **Baseline**

The following information will be collected for all subjects enrolled:

1. History and Physical
2. Cardiac medication list
3. Labs: Creatinine, BUN
4. $CHADS_2$-VASC score
5. HAS-BLED
6. All females of childbearing age will have a urine or serum pregnancy test within 24 hours prior to procedure
7. Cardiac computed tomography angiography (CCTA) will be used to evaluate if subjects' anatomy is favorable for deployment of the SentreHeart Lariat®

5.2 **Left Atrial Appendage Closure Procedure**

The following information will be collected at the time of Procedure

1. TEE evidence of LAA closure
2. Angiographic confirmation of LAA closure
3. Presence/absence of pericardial effusion
4. Amount (# ml) of pericardial drainage
5. X-ray exposure
6. Total amount of contrast used
7. Adverse Events Ass
8. essment

5.3 Follow-up Visits

5.3.1 7 days Post Procedure(-3/+10)

1. Interim history and physical examination
2. Cardiac Medications
3. Chest X-Ray

5.3.2 90 days post procedure (-15/+15)

1. Interim history and physical examination
2. Cardiac Medications
3. Chest X-Ray

5.3.3 180 days Post Procedure (-30/+30)

1. Interim history and physical examination
2. Cardiac Medications
3. Chest X-Ray

4. Either Cardiac computed tomography angiography (CCTA) or Transesophagel Echocardiogram (TEE) to be completed to confirm LAA closure

6. **MATRIX**

	Screening /Baseline	Procedure	7 Day Follow-up (-3/+10)	90 Day Follow-up (-15/+15)	180 Day Follow-up (-30/+30)
History & Physical	X				
EP Consultation	X				
Cardiac Medication	X		X	X	X
Labs: Creatinine & BUN	X				
CHADS2-VASC Score	X				
HAS-BLED Score	X				
Chest X-Ray			X	X	X
TEE		X			X*
CCTA	X				X*
Angiography		X			
Adverse Events Assessment		X	X	X	X

*Either a CCTA or TEE will be completed to confirm LAA closure

7. SUMMARY

7.3.1 **Enrollment:** up to 50 subjects to be enrolled

7.3.2 **Duration of Enrollment:** 180 days (-30/+30)

8. SCREENING

Subjects evaluated for left atrial appendage closure will be screened for inclusion and consented prior to their procedure. During clinical evaluation of the patient, the physician investigator will assess those items described in Table 1. If the anatomy is favorable for placement of the Lariat® device, the procedure will be performed at one of the participating centers. If anatomy is not favorable, the patient will be excluded from the study and managed using best care practices by his or her physician.

A copy of the consent form will be given to the patient and another copy will be placed in the patients chart along with documentation of the consent process.

9. ENROLLMENT

Subjects consented will be tracked by the study team and will be considered enrolled in this study at the time of the start of their left atrial appendage closure procedure. All subjects that are consented who do not undergo left atrial appendage closure with SentreHeart Lariat® will be considered screen failures. Any patients that have a failed attempt at left atrial appendage closure with SentreHeart Lariat® will be tracked through their index hospitalization for safety; their study follow up will be complete at the time of discharge.

Subjects that are approached will be given ample time to assure that this population has the opportunity to carefully read the consent, share the information with family members, and discuss the objective of the study along with any risks/benefits that may be expected. Subjects will have all of their questions answered before signing the consent and taking part in the study. Additionally, information on how to contact the study doctor will be provided in the consent form.

9.3 Screening/Enrollment Log

A log will be maintained that documents subjects screened and those enrolled.

10. WITHDRAWAL

A subject may voluntarily withdraw at any time.

11. END OF STUDY

Enrollment in this study will be completed once a subject completes all of the protocol required 90 day assessments. If a subject is unable to complete these assessments, their enrollment will be completed at the end of the 90 day window unless an appointment has been made to complete an out of window visit for extenuating circumstances. Any patients that have a failed attempt at left atrial appendage closure with SentreHeart Lariat® will be tracked through their index hospitalization for safety; their study follow up will be complete at the time of discharge.

If unsuccessful attempts have been documented to contact and arrange an end of study follow-up visit (90 day), the social security death index will be queried at a later date to confirm the subjects' status at the time of study completion.

12. RISKS/BENEFIT

12.1 Risks and Adverse Event Reporting

The study is a multi-center, prospective outcomes registry. Adverse events will be reviewed, adjudicated and reported per IRB policy

Known risks associated with the SentreHeart Lariat® procedure:

- Pericardial Effusion
- Cardiac Tamponade
- Device Embolization
- Atrioventricular Fistula
- Cardiac Perforation
- Thrombus
- Bleeding
- Bruising/Hematoma
- Arrhythmia
- Pseudoaneurysm
- Valvular Damage
- Stroke
- Conversion to Surgery
- Death

12.2 Minimization of Risks

Patient safety during this study will be the highest priority. The patients will not incur any psychological, social, legal or economic risks by participating in this study.

12.3 Benefits

Left atrial appendage closure with the use of SentreHeart Lariat® may reduce subjects' risk of stroke. Information learned from this study may help in the management of patients with atrial fibrillation and atrial flutter who are at elevated bleeding risk with the use of any OAC therapy.

13 DATA MANAGEMENT

13.1 Data Storage:

An appropriate database will be created and managed in compliance with HIPAA regulations. Data will be stored safely in a secure environment, and maintenance for back-up purposes will be performed on a routine basis to avoid data loss.

13.2 Research Subject Privacy

Patients will be approached discretely and privately by the study coordinator. The discretion of the study coordinator will be used to judge if privacy (from both medical personnel and other persons in the hospital) is ensured during the consent process. The patient will be informed that they can stop the consent process at any time if they feel their privacy is being compromised, and no information will be collected directly from the patient after that point. Patients will be informed that participating / not participating in this study will in no way affect their care and that they are in no way obligated or expected to participate. If the patient agrees to participate, they will be taken through the informed consent process. Upon data collection/acquisition, study identifiers will be encrypted to protect patients' privacy and meet HIPAA regulations, and data will be stored in a secured database while periodic back-up. All hard copy material (summary printouts) will be stored securely and all electronic storage media will be safely stored as per HIPAA regulations. All patient identifiers will be removed from research related documents and a study specific identifier assigned to each subject. Only de-identified data will be used for analysis and only aggregate results will be reported. Only those directly related to the research will be allowed access to subject information.

14 DATA MONITORING

Internal monitoring will be conducted periodically and reviewed by the data monitoring committee. CRFs, source documents, informed consent forms, and study deviations will be included; these findings will be reported to the PI. Deviations will be documented and reported according to IRB policy.

Regulatory documents will be audited by the Baylor Research Institute Department of Research Compliance upon request.

15 STATISTICAL ANALYSIS & DATA MANAGEMENT

Data on the clinical and non-clinical risk factors will be summarized using means, standard deviations (SDs) and percentages. Successful left atrial appendage closure will be reported as a percentage

Table 1. Patient screening tool

1. Atrial fibrillation or atrial flutter documented? ☐ Yes ☐ No
   ☐ Paroxysmal ☐ Short-lasting persistent ☐ Longstanding persistent

2. EP consultation to exclude candidacy for ablation? ☐ Yes ☐ No
   ☐ catheter or ☐ surgical

3. CTA obtained to assess LAA anatomy? ☐ Yes ☐ No
   If yes, was anatomy favorable for this procedure? ☐ Yes ☐ No
   If no, justification for procedure:
   _____
   If no, was second opinion obtained? ☐ Yes ☐ No
   Physician rendering second opinion:_____

4. $CHADS_2$-VASC score _____of 9
   a. CHF _____of 1
   b. Hypertension _____of 1
   c. Age >65 yrs _____of 1
   d. Diabetes Mellitus _____of 1
   e. Stroke or TIA _____of 2
   f. Vascular Disease _____of 1
   g. Age >75 _____of 1 (in addition to age>65)
   h. Sex Category _____of 1 (Male=0; Female =1)

5. $CHADS_2$ score: _____of 6
   a. CHF _____of 1
   b. Hypertension _____of 1
   c. Age >75 yrs _____of 1
   d. Diabetes Mellitus _____of 1
   e. Stroke or TIA _____of 2

6. HAS-BLED SCORE _____of 9
   a. Hypertension _____1
   b. Abnormal renal and hepatic function [2] _____1-2
   c. Stroke _____1
   d. Bleeding tendency/predisposition[3] _____1
   e. Labile INRs on warfarin[4] _____1

[1]Systolic BP >160 mmHg
[2]Renal: serum creatinine >2.25 mg/dl
Hepatic: Bili 2-3x normal and AST/ALT/ALK-P >3x normal or chronic disease (cirrhosis)
[3]History of bleeding or anemia
[4]Time in therapeutic range <60%
[5]Concomitant antiplatelet or NSAID use or excess alcohol

f. Elderly (>65 yr) _____1
g. Drugs or alcohol (1 point each)[5] _____1-2

6. If $CHADS_2$–VASC score<3, or if HAS-BLED score is <3, list justification for procedure:

_____
_____
_____
_____
_____