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State Of The Art In Left Atrial Appendage Ligation - The Lariat

Pramod Janga,[1] Hema Pamulapati,[2] Arun Kanmanthareddy,[1,3] Ajay Vallakati,[4] Sampath Gunda,[1] Sudharani Bommana,[1] Misty Jaeger,[1] Yeruva Madhu Reddy,[1] Dhanunjaya Lakkireddy[1]

[1]Section of Electrophysiology, Division of Cardiology, Cardiovascular Research Institute, University of Kansas Hospital & Medical Center, Kansas City, KS. [2]Department of Internal Medicine, University of Missouri Kansas City, Kansas city, MO. [3]Division of Cardiology, Creighton University School of Medicine, Omaha, NE. [4]Department of Cardiology, Case Western Reserve University/ MetroHealth Campus, Cleveland, OH.

Abstract

Percutaneous left atrial appendage ligation (LAA) techniques have come to the forefront of management of atrial fibrillation (AF) patients who are at high risk of stroke and are unsuitable for oral anticoagulation therapy. LARIAT is a novel percutaneous endo-epicardial ligation technique for LAA exclusion. This technique is increasingly becoming popular for LAA exclusion in AF patients. A few studies have validated the efficacy of LARIAT in mitigating stroke risk in AF patients with contraindications to anticoagulation. Additionally a few studies have suggested that AF burden decreases after the LARIAT procedure. In this review paper we discuss the indications, technique and the latest advances in the LAA exclusion using the LARIAT system.

Introduction

Atrial Fibrillation (AF) is the most common sustained atrial arrhythmia, which results in significant morbidity and mortality.[1] It is currently estimated that the prevalence of AF in the United States is projected to reach around 12 million by the year 2050.[2] The main complications associated with AF are stroke and cardiomyopathy.[3] AF increases the risk of hospitalizations and worsens the quality of life. The increasing prevalence of AF and the complications associated with it results in increasing socio-economic and healthcare burden on the society, of which stroke accounts for the majority of the burden. Patients suffering from stroke due to AF have prolonged hospital stay and are more likely to suffer from long term disabilities.[4,5]

Oral anticoagulation has been the preferred strategy for decreasing stroke risk in AF patients. However use of these agents is associated with increased risk for bleeding and is not suitable for those with contraindications to oral anticoagulation. Surgical LAA exclusion was commonly done during Cox-Maze procedure and mitral valve surgery. Progressively newer and less invasive techniques have been developed for LAA exclusion. LARIAT is a novel, minimally invasive endo-epicardial LAA exclusion technique and in this review article we discuss the rationale for LAA exclusion, LARIAT technique and its advantages compared to other LAA exclusion strategies.

Abbreviations:

AF-Atrial Fibrillation; LAA-Left Atrial Appendage; LSPV- Left Superior Pulmonary Vein; NOACS- Novel oral anticoagulants, ANP – Atrial Natriuretic Peptide.

Key Words:

Left Atrial Appendage, Atrial Fibrillation, Stroke, LAA Exclusion, LARIAT.

Disclosures:
None

Corresponding Author:
Dhanunjaya Lakkireddy MD, FACC, FHRS
Professor of Medicine
Director, Center for Excellence in Atrial Fibrillation & Electrophysiology Research
Bloch Heart Rhythm Center – Mid America Cardiology
KU Cardiovascular Research Institute- University of Kansas Hospital & Medical Center
3901 Rainbow Blvd, Kansas City, KS 66160

LAA Morphology and Functions

The LAA is a remnant of the primitive left atrium, which is formed during the 3rd week of gestation. The LAA is a long tubular, often multi-lobed and trabeculated structure, which opens into the left atrium by means of an ostium between the left superior pulmonary vein and the mitral annulus.[6] Morphologically, the LAA can be classified into 4 different types based on its external appearance: 1. Wind Sock: In this type, the primary lobe is the dominant part of the LAA. 2. Chicken Wing: In this type of LAA, the dominant lobe is bent at an angle at some distance from the ostium. 3. Broccoli: The LAA has complex internal characteristics like the lobes of a broccoli. 4. Cactus: The LAA has a dominant lobe and secondary lobes extend from the central lobe.[7] Internally the LAA morphology is complex and highly heterogeneous. This internal morphology is the ideal substrate for thrombus formation in AF wherein there is reduced contractility of the left atrium. The ostium of the LAA is located between the left superior pulmonary vein and the mitral valve annulus. Physiologically, the LAA acts as a decompression chamber during states of elevated left atrial filling pressures. The endothelial lining of the LAA also contains cells rich in atrial natriuretic peptide (ANP). The LAA may therefore help maintain fluid balance in states

of volume overload.

Rationale for LAA Occlusion

Nearly 90% of thrombi in non-valvular AF originate from the left atrial appendage (LAA).[8] The anatomical and physiological characteristics of the LAA make it highly thrombogenic, especially during AF. Oral anticoagulation is effective in mitigating stroke risk in AF patients.[9] Until a few years ago, warfarin was the only drug available for oral anticoagulation and subsequently novel oral anticoagulants (NOACS) have been developed and are increasingly being adapted in the management of patients with AF. However there is increased risk of bleeding associated with the use of warfarin and the NOACS. There is a 1.4% annual risk of major bleeding with the use of warfarin.[10] Additionally, there is a high rate of discontinuance of warfarin. Adverse effects and limitations in lifestyle due to warfarin use are the main reasons for discontinuation of warfarin. Frequent monitoring of INR is needed in warfarin users and this imposes additional restrictions on lifestyle. Further, even in compliant patients the INR is often not within the therapeutic range. The Stroke Prevention using ORal Thrombin Inhibitor in atrial Fibrillation (SPORTIF) trials reported INR levels within therapeutic range of 2-3 only 67.5% of the time and that number is even lower in the community setting.[9]

The NOACS overcome several of the shortcomings associated with the use of warfarin. These agents do not need monitoring and do not have any interactions with food and therefore have fewer limitations on lifestyle. However, bleeding is still a concern with the use of these agents. Surgical LAA exclusion is a possibility and this is done during the Cox-Maze procedure for surgical treatment of AF and also during mitral valve surgery.[11] Over the years, various endocardial and epicardial percutaneous LAA exclusion techniques have been developed. The endocardial LAA exclusion is done using WATCHMAN and Amplatzer Cardiac Plug devices; several others are still in development.[12-14] The epicardial LAA exclusion techniques include TIGERPAW and AtriClip.[15,16] LARIAT is a novel technique wherein the LAA is excluded percutaneously using a combined endo and epicardial approach and does not leave any hardware behind in the heart.

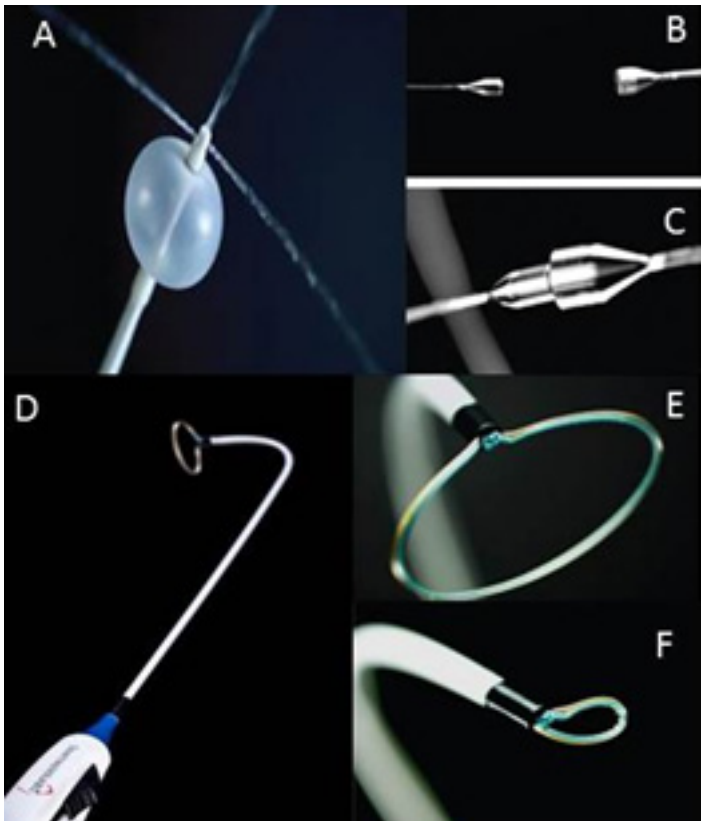

Figure 1: LARIAT suture device components: A. Large occlusion balloon catheter B. Magnet-tipped guidewires C. Magnetic Guidewires aligned D. LARIAT suture delivery device E. LARIAT suture before tightening F. LARIAT suture after tightening

Indications for LARIAT Procedure

Currently the LARIAT procedure is being performed in patients with AF who have a high risk of stroke as assessed by the CHADS2 score and have contraindications to oral anticoagulation such as recurrent bleeding, history of bleeding in critical areas (brain, cavities) and patients who are at high risk of falls. Also, the LARIAT procedure may be performed in patients in whom oral anticoagulation is ineffective in preventing stroke.

Pre-Procedural Assessment

Anatomical assessment of the LAA is a critical component of the pre-operative assessment. In order to determine eligibility, the patient being considered for LARIAT procedure undergoes a cardiac CT. These CT images are then processed to construct a 3D CT image of the heart. The size, shape, morphological characteristics and orientation of the LAA are assessed for these images. The maximum diameter of the LARIAT suture is 40 mm and therefore the LAA maximal width cannot exceed 40 mm. Posteriorly directed LAA's are also not amenable for LARIAT because the epicardial guidewire and the LARIAT suture cannot be engaged from the epicardial route. Additionally if the LAA is in close proximity to the pulmonary artery or trunk, there is increased risk of rupturing these vessels and hence this procedure is usually avoided in such patients. Additionally, this procedure cannot be done in patients with pectus excavatum, prior history of cardiac surgery, thoracic surgery, chest radiation therapy and pericarditis because of the adhesions.[17,18]

A transesophageal echocardiography (TEE) is also recommended preoperatively, to assess the size of the LAA and also for exclusion of the left atrial- or LAA-thrombus. If a patient has thrombus, then anticoagulation is continued until the resolution of thrombus and then they can be considered for the LARIAT procedure once the thrombus resolves. All the patients undergoing this procedure need to be on oral anticoagulation for a few weeks before and after the procedure.

LARIAT Procedure

Bartus et al. first demonstrated the feasibility and safety of the LARIAT procedure in humans.[19] The LARIAT system consists of the following components (Figure 1):

1) LARIAT suture delivery device
2) Magnet-tipped guidewires (FindrWIRZ® Guide Wire System)
3) Large occlusion balloon catheter (EndoCATH®)
4) SofTIP™ guide cannula
5) SureCUT ™ suture cutter

Technique

The procedure is performed under general anesthesia and in a hybrid suite with cardiothoracic surgical backup. Immediately prior to the procedure, a TEE is performed to rule out left atrial and LAA thrombus. During this procedure, the LAA is visualized in multiple planes to accurately assess and confirm the dimensions and

morphology of the LAA. Continuous intraoperative TEE is done for the entire duration of the LARIAT procedure. During the procedure anticoagulation is maintained by means of heparin drip and the ACT should be maintained at >250 seconds.

Next the groin area is prepared and femoral vein access is obtained using the modified Seldinger technique. After obtaining the femoral vein access, a trans-septal sheath is introduced into the femoral vein and the distal tip is positioned in the right atrium. Next a Brockenbrough needle is introduced into this sheath. The inter-atrial septum is visualized by means of the TEE and under its guidance trans-septal puncture is performed. The Brockenbrough needle is carefully positioned in the distal part of the inter-atrial septum. The location of trans-septal puncture should be mid-low on the interatrial septum and should be directed posteriorly in order to gain easy access to the LAA. After visualization of the Brockenbrough needle on the TEE, the trans-septal puncture is performed. Immediately after the trans-septal puncture, an additional 5,000-10,000 Units of Heparin is given intravenously to maintain the ACT >250. Confirmation of the trans-septal puncture is verified by means of left atriogram as well as a bubble study.

A pigtail catheter is then advanced over the guidewire into the LAA and the left atrial appendogram is done to visualize the LAA. Size and orientation of the LAA are again reviewed on the appendogram. After this an occlusion balloon catheter (EndoCATH®) is advanced into the left atrium and the LAA. A magnet tipped guidewire (FindrWIRZ® Guide Wire System) is then introduced into the occlusion balloon catheter and advanced into the LAA. The 15mm occlusion balloon has distal perfusion holes for angiographic purpose and LAA angiogram can be performed to mark the appendage and evaluate the position of endocardial guide wire. The endovascular magnet tipped guidewire is then carefully navigated to the most distal part of the prominent lobe of the LAA and is stabilized.

Next steps involve obtaining the epicardial access. The subxiphoid area is infiltrated with local anesthetic and a micropuncture pericardiocentesis needle is used to gain access to the pericardial space under fluoroscopic guidance. The micropuncture needle is directed superiolaterally towards the left shoulder and about10-15˚ posteriorly under fluoroscopy guidance. The needle is carefully advanced and radiocontrast dye is injected through the needle to verify its position once it enters the pericardial space. After confirming the position of the needle with multiple fluoroscopy views (RAO and LAO views), a guide wire is then carefully threaded into the pericardial space through the micropuncture needle. Therafter, serial dilators are used to dilate the epicardial access route and finally a 13 F soft tipped guide cannula is advanced into the pericardial space.

The epicardial magnet tipped guide wire is then introduced into the pericardial space through the epicardial soft tipped cannula. This magnet wire is then carefully navigated towards the endocardial magnet tipped guidewire until both the wire tips attach to each other and align coaxially. This is the most important step of the procedure. The alignment is reviewed on fluoroscopy in multiple projections (Figure 2).

Next the LARIAT suture delivery system is then carefully advanced over the epicardial magnet tipped guidewire. The advancement of the suture system is monitored carefully by means of fluoroscopy. If the magnets detach anytime during this process, then the LARIAT suture system is retracted and the magnets will be reengaged. Once this alignment occurs, the LARIAT suture system can be redeployed over the epicardial guidewire. This suture system is carefully advanced over the LAA over the coaxially aligned endo-epicardial magnet tipped wires until it reaches the ostium of the LAA. The EndoCATH® balloon is used as a reference for positioning the LARIAT snare at the ostium of the LAA (Figure 3). The position of the LARIAT snare is then checked in multiple views on fluoroscopy and also on the TEE. This is a very important step before deploying the suture. Once it is confirmed that all the lobes of the LAA are beyond the LARIAT suture, then the suture is deployed and tension is applied to tighten the suture.

After deploying the suture, once again an atriogram is done to visualize the exclusion of the LAA. This is again verified by means of TEE. If this position is considered satisfactory, then the endocardial magnet tipped guidewire and the balloon catheter are withdrawn and further tension is applied to the LARIAT suture for several minutes using TenSURE suture tightener. If this position is not found to be satisfactory, then the LARIAT suture can be released and redeployed at a satisfactory location. Repeat visualization of the LAA is done on the TEE to verify the location of the suture (Figure 4). A left atriogram is also performed to check for complete exclusion of the LAA. Once this is verified, the suture is cut off using a suture cutter (SureCUT™ Suture Cutter). All the wires and sheaths are then retracted and a pericardial drain is placed and will be left in place for the next 24-48 hours.

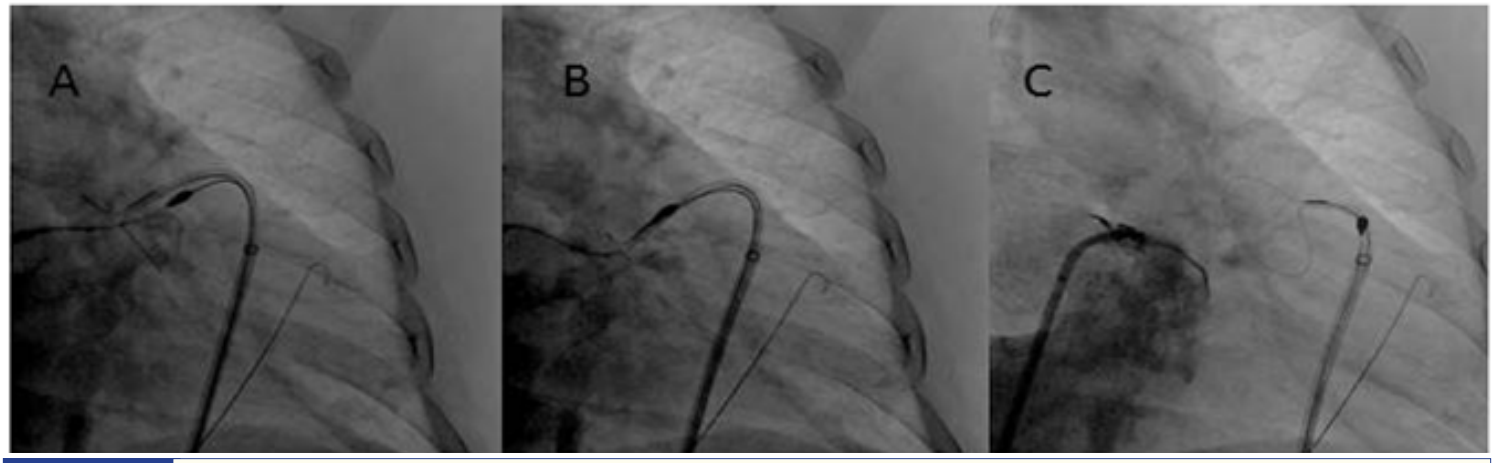

Figure 2: Fluoroscopic images demonstrating LAA exclusion by LARIAT procedure. A. Deployment of LARIAT suture delivery system over coaxially aligned endo and epicardial magnet tipped guidewires. B. Tightening of the LARIAT suture. C. Exclusion of the LAA after the deployment of LARIAT suture as confirmed by left atriogram

Post-Procedural Management

After the procedure the patients are usually monitored in the hospital for 48-72 hours. The pericardial drain is typically removed after 24-48 hours. Post-procedure colchicine is recommended to decrease pericardial pain. Additional pain management involves a combination of non-steroidal anti-inflammatory drugs and narcotics for adequate pain control. A repeat echo may be done post-operatively to monitor for pericardial effusion. Once the pericardial drain is removed, the patients are monitored for 24 hours and then discharged home.

Follow up

Recommended follow up of patients undergoing LARIAT procedure is at 1, 3, 6 and 12 months after the LARIAT procedure. Complete endothelialization of the surface of the excluded LAA is expected to be completed by 45 to 90 days after the LARIAT procedure. Inflammatory changes at the ostium of the LAA are anticipated from the deployment of the suture around the ostium and therefore routine anticoagulation is recommended during this time to decrease thrombotic risk. In those patients in whom oral anticoagulation is absolutely contraindicated, antiplatelet agents may be tried. A follow up TEE is recommended 45-90 days after the procedure to assess adequate sealing of the LAA, and if no residual leaks are found then the patient can discontinue oral anticoagulation. Subsequently these patients can be followed up in the clinic and a repeat TEE should be done in 6-12 months to check for any thrombus formation in the LA and to evaluate sealing of the LAA. Follow up imaging after 1 year can be done at the discretion of the operator.

Efficacy of LARIAT

The clinical efficacy of LARIAT in decreasing stroke risk was evaluated by Lee et al. These findings were presented at the Heart Rhythm Society annual scientific sessions 2014. In this multicenter study, a total of 138 patients were followed up for a total of 300.5 patient years.[20] At the end of the follow up period, the incidence of stroke and systemic embolism was 1.3% per year.[20] The stroke rate was significantly lower than that observed in the National Registry of AF (3.9%).[20] The combined end point of stroke, systemic embolism and death was 3.3% per year.[20] The above data therefore suggests that LARIAT is effective in decreasing stroke risk in AF patients with contraindications to anticoagulation.

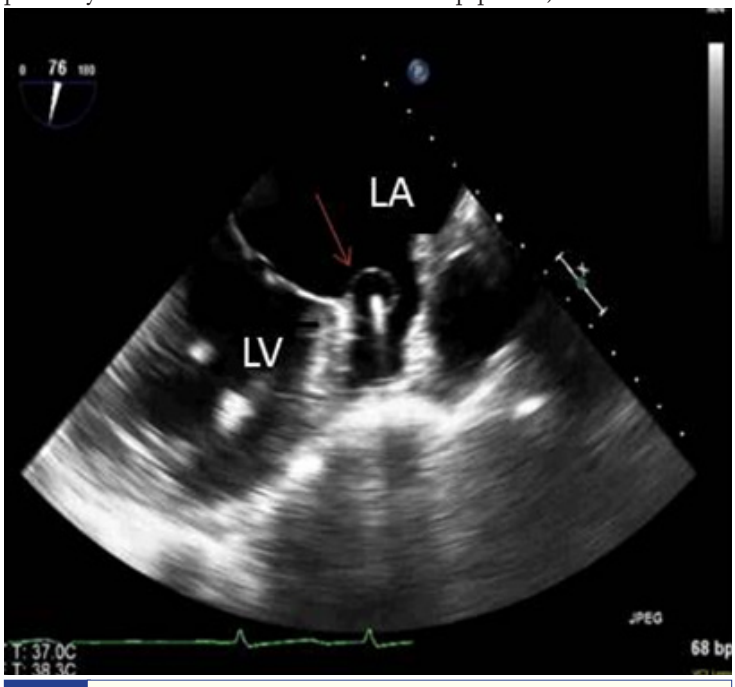

Figure 3: Echocardiographic image showing the endocardial balloon catheter within the LAA prior to deployment of the LARIAT suture

LA-Left atrium, LV-Left ventricle

Advantages

1. This is a minimally invasive procedure and therefore the patients can recover faster from the procedure compared to other surgical or mini thoracotomy based approaches such as the AtriClip.[15]

2. In this procedure an epicardial suture is deployed and there are no endovascular devices left behind in the LAA and therefore, theoretically, the risk of thrombus formation over the device or infections associated with the device should be low to none.[18]

3. There is no risk of device embolization like in the case of other implantable devices. When compared to implantable devices, with LARIAT device, there is decreased risk of device dislodgement or embolization and device failure.[21]

4. LAA also contains triggers for initiating AF and therefore exclusion of the LAA by means of LARIAT can also eliminate the AF triggers. Evidence to this effect has been seen in a few studies.[22] The unipolar LAA voltage decreased from 1.1 ± 0.53 mV to 0.3 ± 0.38 mV after the LARIAT procedure.[22] Similarly, the bipolar LAA voltage decreased from 4.7 ± 2.83 mV to 0.6 ± 0.27 mV.[22] In the LAALA-AF study, the efficacy of LARIAT procedure as adjunct to AF ablation was compared with patients undergoing only AF ablation.[23] In this study, the AF recurrence was 35% in patients undergoing LARIAT and AF ablation compared to 55% in patients undergoing AF ablation only.[23] The above studies clearly suggest the role of LAA as a trigger for AF and LARIAT procedure offers the benefit of eliminating these triggers.

Peri-procedural Complications

Chest pain is the most common complication after the LARIAT procedure. Chest pain after the procedure was reported by 23.5% of the patients lasting for less than a day.[21] Two of these patients were found to have acute pericarditis and were treated with non-steroidal anti-inflammatory drugs.[21] Perforation of the heart can occur while obtaining pericardial access, during engagement of the epi and endocardial magnet tipped guidewires and while deploying the LARIAT suture. This is an infrequent but fatal complication and requires immediate thoracotomy. Complications related to the procedure were seen in 3 (3.4%) of the patient's in one study.[21] Two patients had pericardial access related complications; one patient had a right ventricular puncture and the other patient had laceration of the superficial epigastric vessel.[21] In one other patient, perforation of the myocardium occurred during trans-septal catheterization.[21] Therefore, this procedure needs to be performed in a hybrid suite with cardiothoracic surgery backup. Pericardial effusion can occur from irritation of the pericardium during the procedure and also due to manipulation of the guidewires and trauma associated with the deployment of the LARIAT suture. This effusion is highest during the first 24-48 hours after the procedure and thus a pericardial drain is left in place at the conclusion of the procedure. Tamponade can also occur from perforation of the heart during the LARIAT procedure.

Transient ischemic attack or stroke is a possibility due to deployment of catheters in the left atrium and therefore anticoagulation with heparin is recommended during the entire procedure to maintain ACT > 250 seconds. Denovo thrombus formation post LARIAT

procedure has been reported in a few cases.[24-27] Thrombus formation was seen in 6 patients in whom thrombus was detected during follow up TEE. In 3 of those cases, thrombus was seen at the endocardial surface of LAA closure site in the left atrium.[24-26] The thrombus was reportedly in the remnant stump of LAA after incomplete exclusion in the remaining 3 cases.[24,27] There were no clinical embolic events reported from the above studies and thrombi were reported to be resolved after anticoagulation treatment.[24-27] Due to this increased and unpredictable risk of thrombus formation post-LARIAT, anticoagulation is recommended for a period of up to 90 days or sooner if the follow up TEE demonstrates complete sealing of the LAA during follow up. Other complications include access site complications such as groin hematomas and pseudo aneurysms.

Post-LARIAT Leaks in the LAA

After deploying the LARIAT suture, complete sealing and endothelialization of the ostium of the LAA is expected to be complete by 45-90 days. However, incomplete sealing with remnant leaks may be a possibility in a few of them. Complete sealing of the LAA defined as leak <1 mm was seen in 95% of the subjects undergoing LARIAT procedure at 90 days and this improved to 98% at 1 year.[21] Leaks varying in size between 1-3 mm was observed in 5% of the LARIAT patients at 90 days and by 1 year only 2% of the subjects had this remnant leaks.[21] There have been isolated case reports where the leaks have been > 3 mm and various innovative approaches have been used to seal off these leaks. Yeow et al. reported a successful closure of residual leak after LARIAT procedure by GoreR HelexR Septal Occluder, which was primarily designed for occlusion of atrial septal defect.[28] In another case series, Mosley et al reported closure of the LAA leak following LARIAT procedure using AVP-4 (Amplatzer Vascular Plug).[29] In their case series, 3 patients had successful exclusion of the LAA leak using the AVP-4 plug.[29]

In our own experience, leaks less than 5 mm in size after the LARIAT procedure was managed safely using the atrial septal defect occluder device. We used the 5 mm atrial septal occluder device in 5 patients who had a mean leak size of 4.3 ± 0.6 mm. Successful closure of the leak was observed in all of them. In another patient, we did a redo LARIAT procedure and were able to successfully exclude the LAA without any residual leak.[30]

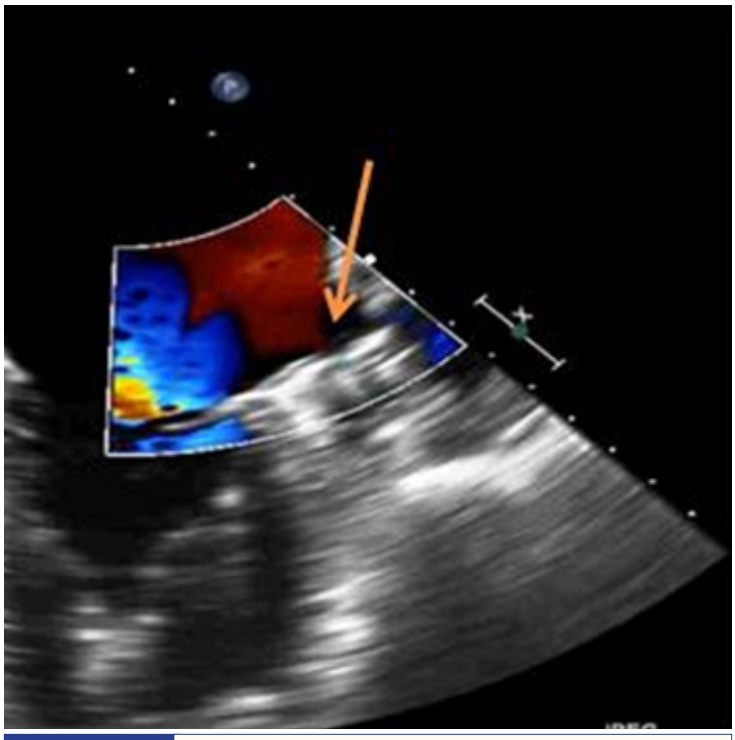

Figure 4: 2D Doppler Echo image demonstrating complete exclusion of LAA from the rest of circulation

Theoretically any residual communication between the left atrium and LAA should pose an increased risk for stroke. This risk would probably vary with the size of the leak and the flow parameters across the LAA orifice. However due to limited experience with the LARIAT device, the correlation between stroke risk and the size of the leak is not accurately known.

Conclusion:

LAA occlusion has been an area of tremendous interest for electrophysiologists, interventionists and cardiothoracic surgeons alike, with many catheter based and surgical procedures being developed and tested. It only augurs well for the patients who are at high risk of stroke and have contraindications to anticoagulant therapy that the newer procedures and techniques prove to be safe and efficacious. LARIAT procedure for LAA occlusion is a novel percutaneous technique and is increasingly being adapted. The procedure needs to be performed by highly skilled operators and should always be performed with surgical back up support. Besides decreasing the risk of stroke, it appears to offer the added advantage of elimination of the electrical triggers of AF. The safety and efficacy of the LARIAT procedure has been demonstrated in a few studies.

This technique is yet to be adapted by the major cardiology professional organizations into the clinical guidelines for the management of AF.

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