CONTROVERSIES IN ELECTROPHYSIOLOGY

REVIEW ARTICLE

Left Atrial Appendage Closure for Stroke Prevention is Safe and Effective in Selected Patients with Atrial Fibrillation

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ABSTRACT. The left atrial appendage (LAA) is implicated as a source of thrombus in the majority of patients with atrial fibrillation (AF) and embolic stroke. Therapeutic anticoagulation (AC) is the mainstay of treatment for stroke prophylaxis in AF. Despite adherence to AC, a significant number of patients are still subtherapeutic. In addition to this, several patients are ineligible for AC because of various reasons, including but not limited to high bleeding risk, ongoing bleeding, and non-compliance. These challenges associated with AC led to efforts looking at mechanical isolation of the LAA. Various endocardial and epicardial devices have been tried for mechanical isolation of the LAA, with variable success. The WATCHMAN™ (Boston Scientific, Maple Grove, MN) is the first endocardial device that received FDA approval as an alternative for warfarin for stroke prophylaxis in AF. The WATCHMAN™ (Boston Scientific) is not approved for AC-ineligible patients. The LARIAT™ (SentreHEART, Inc., Redwood City, CA) is an epicardially deployed device that has been proposed for AC-ineligible patients. Although not FDA approved, its safety and efficacy had been established in large prospective registries. The current review examines the current literature on AC and LAA exclusion devices in a comparative fashion. The protean effects of LARIAT™ (SentreHEART, Inc.) on rhythm and neurohormonal control are also reviewed. We conclude that LAA exclusion devices are an excellent alternative to AC for stroke prophylaxis in AC-eligible (WATCHMAN™, Boston Scientific) and ineligible patients (LARIAT™, SentreHEART).

KEYWORDS. left atrial appendage closure, novel oral anticoagulants, stroke, warfarin.

Introduction

Emolic stroke is the most dreadful complication of atrial fibrillation (AF). It is estimated that the annual incidence of stroke is 780,000 cases per year.1 Stroke related to AF results from embolic thrombi originating in the left atrium. It is estimated that the embolic stroke from AF occurs in 36.2% of patients over the age of 80.2 AF-related stroke is often more disabling than other types of strokes.3,4 Therapeutic anticoagulation (AC) is the most commonly used prophylactic measure against thromboembolic strokes from AF. Warfarin was the most commonly used AC until the emergence of novel oral anticoagulants (NOACs). Oral AC with warfarin or NOACs has several challenges, including but not limited to bleeding complications, non-compliance, subtherapeutic levels, and lack of an antidote to NOACs (except for dabigatran). The risk of complications associated with
AC is even higher in elderly patients. Elderly patients with comorbidities are at a particularly increased risk for both stroke and bleeding. These limitations of AC led to the emergence of alternative therapies for stroke prophylaxis in patients with AF.

AF patients are also predisposed to silent cerebral ischemia, which contributes to cognitive impairment and dementia. The prevalence of silent cerebral ischemia is reported to be higher in patients with AF than in patients without AF. Although the exact mechanism is unclear, possible mechanisms include microemboli from suboptimal AC, cerebral hypoperfusion from irregular heart rhythm, and cerebral microbleeds, which increase with age and with AC use. Thus mechanical exclusion of the left atrial appendage (LAA) may offer protection against such undesirable consequences of AF and its treatment.

The LAA is an embryologic remnant of the left atrium that has been shown to be the predominant source of arterial thrombi in patients with AF. Based on this knowledge, many devices and techniques have been developed to exclude the appendage from the circulation thereby preventing thrombi from entering the systemic circulation. LAA closure can be performed surgically or percutaneously. The percutaneous approaches can be classified as endocardial, epicardial, or hybrid endocardial-epicardial procedures. Currently, the WATCHMAN™ (Boston Scientific, Maple Grove, MN) implant is the only endocardial LAA exclusion device that has been approved as an alternative to warfarin for stroke prevention in AF by the FDA. Other LAA closure devices such as the LARIAT™ (SentreHEART, Inc., Redwood City, CA) and the AMPLATZER™ cardiac plug (ACP) (St. Jude Medical, St. Paul, MN) have been used off label for this purpose in the United States. Single and multicenter prospective observational studies have reported promising results.

With careful patient and device selections, LAA closure is a promising alternative for patients who are either high risk for bleeding complications or are ineligible for AC. Such patients should be offered LAA exclusion device therapy as a first-line option for prophylaxis against thromboembolic strokes. Although LAA closure is considered invasive and associated with procedural complications, safety has improved dramatically over the years. Some studies have suggested that this approach may be cost effective in the long run when compared with long-term AC.

LAA exclusion therapies are evolving. Improvements in device design and increasing operator experience have significantly improved the procedural safety profile of LAA exclusion devices. It is imperative that patients be educated regarding the risks, benefits, and alternatives of LAA occlusion devices. We will review some of the main limitations of AC and elucidate the efficacy and safety profile of LAA closure.

**Limitations of oral anticoagulants**

**Non-compliance**

It is estimated that 18–20% of patients with AF are not on AC for various reasons. This puts them at risk for stroke. Although not all bleeding warrants permanent discontinuation of AC, minor bleeding and fear of further bleeding often leads to discontinuation of AC. Only 50–60% of patients on warfarin maintain therapeutic international normalized ratio (INR). According to the Fibrillation Registry Assessing Costs, Therapies, Adverse events and Lifestyle study (FRACTAL), the warfarin discontinuation rate was 20% over a 2.5-year period. Despite the ease of use and predictable anticoagulant effects relative to warfarin, even the NOAC discontinuation rate over 20-month follow-up is as high as 37% (Table 1).

**Concomitant use of dual antiplatelet therapy**

Coronary artery disease (CAD) is a common comorbidity in AF patients. Several patients with CAD require dual antiplatelet therapy following coronary artery stent placement. The concomitant use of AC in these patients significantly increases risk of bleeding. In a large retrospective study of more than 10,000 elderly patients, use of antiplatelets in combination with oral anticoagulants was associated with a threefold increase in intracranial hemorrhage.

**Drug and food interactions of warfarin and NOACs**

Warfarin is associated with several food and drug-drug interactions. Minor dietary changes or institution of other pharmacotherapy can lead to either sub- or supratherapeutic levels of AC. NOACs are comparatively better in this regard but are still not immune to such interactions. Unfortunately, stroke can still occur in some patients despite optimal AC with therapeutic INR.

**Side effects of warfarin and NOACs**

As with any pharmacotherapy, anticoagulants have side effects. Although rare, warfarin has been shown to cause skin necrosis. Dabigatran is associated with frequent gastrointestinal side effects such as dyspepsia. Rivaroxaban is associated with musculoskeletal pain in some patients. Although NOACs have an advantage of lower risk for intracranial hemorrhage (ICH), they are associated with higher risk for gastrointestinal (GI) bleed compared to warfarin.

**Cost of NOACs**

NOACs are an excellent alternative to warfarin. They potentially can increase compliance and provide more

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Discontinuation rate in the study (%)</th>
<th>Major bleeding rate per year (%)</th>
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<tbody>
<tr>
<td>Dabigatran (150 mg)</td>
<td>21</td>
<td>3.1</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>24</td>
<td>3.6</td>
</tr>
<tr>
<td>Apixaban</td>
<td>22</td>
<td>2.1</td>
</tr>
<tr>
<td>Edoxaban (60 mg)</td>
<td>34</td>
<td>2.8</td>
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predictable AC. However, the cost of NOACs tends to be prohibitive for many patients and often leads to sudden discontinuation by patients. This is a problem especially in those with sporadic and unpredictable insurance coverage. Owing to a shorter half-life, abrupt discontinuation of NOACs may put patients at a high risk of thrombosis.24,25

**Lack of specific targeted reversal agents for majority or NOACs**

With the exception of dabigatran, currently there are no reversal agents for NOACs in life-threatening situations such as an intracranial bleed or trauma. This raises a serious concern in patients who are on NOACs when AC needs to be reversed in an emergency situation.

**Safety and efficacy of the left atrial appendage closure devices**

Currently there are two methods for LAA exclusion: surgical and percutaneous. The surgical approach involves incision, stapler exclusion, or suture exclusion. Percutaneous methods include endocardial, epicardial, and endo-epicardial devices. For the purpose of this article, we will focus on devices that are currently available in the United States.

**The WATCHMAN™ implant system**

The WATCHMAN™ (Boston Scientific) device is an endocardial LAA closure device that is implanted via transseptal access achieving occlusion of the LAA at the level of the ostium.26 Currently, the WATCHMAN™ (Boston Scientific) is the only FDA-approved LAA closure device used for stroke prevention in AF patients. It is also the only device that has been studied in two randomized clinical trials. The PROTECT-AF trial showed non-inferiority of the WATCHMAN™ (Boston Scientific) when compared with warfarin. In this trial, the procedural complications rate was 12%. Complications included pericardial effusion requiring drainage, embolic stroke, device migration, and device sepsis.27 The PREVAIL trial was designed to document improved safety and efficacy of the WATCHMAN™ (Boston Scientific) device.28 The 7-day procedural complication rate was 4.5% with a 95.1% success rate. In the PREVAIL trial, the primary efficacy endpoint of stroke, systemic embolism, cardiovascular death, and unexplained death was similar between the WATCHMAN™ (Boston Scientific) and the warfarin groups at 18 months, but the prespecified non-inferiority margin was not achieved, although the late ischemic primary efficacy endpoint of stroke and systemic embolism after 7 days of randomization met the non-inferiority criteria.28 These results could be due to the lower than expected event rates in the warfarin groups.29 In both of these trials, patients were able to tolerate short-term AC with warfarin for 45 days. This trial met the criteria for the safety endpoint, with more than a 50% reduction in complication rates.

In patients with absolute contraindications to AC, the ASAP study (Aspirin Plavix Feasibility Study), which was a non-randomized prospective study in the absence of a control arm, showed that the WATCHMAN™ (Boston Scientific) can be safely deployed without short-term warfarin therapy after implant. In this study, aspirin and Plavix were used for 6 months instead of oral anticoagulants for 45 days. The all-cause stroke rate was 2.3% per year. The preliminary results from ASAP revealed that the ischemic stroke rate was less than expected based on historical risk of patients with similar CHADS2 and CHA2DS2-Vasc scores (7.4% per year).30,31 This study also demonstrated a major complication rate of 8.7%, which is lower than the PROTECT AF trial. Long-term safety has been well studied in the case of the WATCHMAN™ (Boston Scientific) device. Recently, a single center prospective study evaluated long-term safety up to 5 years in patients implanted with the WATCHMAN™ (Boston Scientific) device. In this study, 25% patients who were not eligible for oral AC were given aspirin and clopidogrel for 6 months. The annual rate of transient ischemic attack (TIA) or stroke was 1.4% and the bleeding complication rate was 2.1%. Procedure-related complications occurred in 8.8%. Three patients had pericardial effusions with successful pericardiocentesis, four patients had non-hemodynamically significant pleural effusion, one patient had allergic exanthema, and one patient had post-procedural femoral bleeding.32

**AMPLATZER™ cardiac plug**

The ACP is an endocardial device that is a modification of the Amplatzer septal occluder originally designed for atrial septal defects.26 In a pilot study of 52 patients who could not tolerate warfarin, the implant success rate was 98.1%.10 There were no peri-procedural strokes. Single or dual antiplatelet therapy was used as tolerated. The main complications were device embolization (1.9%), and pericardial effusion (1.9%). At mean follow up of 20 ± 5 months, the rates of death, stroke, systemic embolism, pericardial effusion, and major bleeding were 5.8%, 1.9%, 0%, 1.9%, and 1.9% respectively. The ACP has also been used as an adjunct to other LAA occlusion procedures such as closing residual leaks post LARIAT® (SentreHEART, Inc.).33 Recently Tzikas et al.34 did a large multicenter study to investigate the safety and efficacy of ACP for stroke prevention in patients with AF. In this study of 1,047 patients from 22 centers, procedural success was 97.3% and the peri-procedural complication rate was 4.97%. At 13 months of follow-up, 0.9% patients had stroke and 0.9% had a TIA. The annual systemic thromboembolic risk was 2.3%. Major bleeding occurred in 1.5% of patients.34 In this trial, the post-procedural antiplatelet regimen consisted of aspirin 80–100 mg and clopidogrel 75 mg daily for 1–3 months and then only aspirin 80–100 mg for at least another 3 months. The choice and duration of antiplatelet therapy were individualized according to the patients’ medical history, indication of LAA closure, and physician preference.34
Surgical exclusion of the left atrial appendage

AF is the most common arrhythmia encountered after cardiac surgery. Previous studies indicated 20–50% of patients develop postoperative AF in early postoperative period, which can increase mortality and morbidity. Echahidi et al. reported that the incidence of postoperative stroke was 3.2% after coronary bypass surgery, 2.8% after valve surgery, and 6.7% after coronary artery bypass grafting plus valvular surgery. Surgical LAA exclusion techniques could reduce this postoperative risk. Surgical LAA closure has been performed since the 1930s in conjunction with mitral valve surgery. Surgical exclusion of the LAA is done either through the use of staples or sutures or by deployment of an AtriClip (AtriCure, Mason, OH).

LAA exclusion may reduce postoperative cerebrovascular accident (CVA) in patients undergoing cardiac surgery regardless of history of preoperative AF. A prospective observational study by Kato et al. found that an additional LAA exclusion procedure at the time of cardiac surgery can reduce postoperative stroke, especially in patients with low CHADS-VASc score. Surgical techniques are fraught with incomplete closures. For instance, endocardial suture closure may result in thrombus formation from incomplete closure. The 2014 ACC/AHA guidelines recommended total excision of the LAA during cardiac surgery to avoid this problem.

Studies have shown that surgical LAA exclusion is associated with high failure rates. This is due to the probability of leaving a residual stump and persistent flow into the appendage in the case of suture and staple exclusion; partially closed LAAs are more prone to thrombose. A study by Kanderian et al. in assessing the success rate of various surgical techniques found that overall surgical LAA closure was unsuccessful in nearly 60% of patients. Persistent flow using transesophageal echocardiography (TEE) was found in 60% of suture exclusions and in 58% of staple exclusions. Of all techniques, excision was found to be the most effective with a success rate of 73%.

AtriClip

The AtriClip (AtriCure) is a relatively new surgical LAA closure device that was FDA approved in 2009. It is the most widely used LAA exclusion device through the minimally invasive epicardial approach. The data from initial series demonstrated successful closure in 60 of 61 patients at 90 days of follow-up. A multicenter trial to evaluate the safety of AtriClip (AtriCure) in patients who cannot tolerate oral AC is underway.

LARIAT

The LARIAT® (SentreHEART) is a percutaneous LAA closure technique that combines an endocardial approach through transseptal access and suture ligation from the epicardium through epicardial access. The device is currently only approved for soft-tissue approximation; however, it has been used for LAA exclusion worldwide. Although there has been no randomized trial, many single and multicenter studies have published positive results.

A large multicenter registry of 712 consecutive patients undergoing LAA ligation with the LARIAT® (SentreHEART, Inc.) at 18 US hospitals showed successful deployment in 682 patients (95.5%). Complete closure was achieved in 669 patients (98%), while 13 patients (1.8%) had a trace leak (<2 mm). There was one death related to the procedure. This patient died of multi-system failure after cardiac perforation and surgical repair that occurred during the first 30 days of the procedure. Ten patients (1.44%) had cardiac perforation necessitating open heart surgery, while another 14 (2.01%) did not need surgery. Over time, the risk of cardiac perforation decreased significantly with the introduction of newer access techniques such as the use of the micropuncture (MP) needle for pericardial access.

In this study, delayed complications (pericarditis requiring >2 weeks of treatment with non-steroidal anti-inflammatory drugs/colchicine and pericardial and pleural effusion after discharge) occurred in 34 (4.78%) patients, and the risk decreased significantly with the peri-procedural use of colchicine. The use of colchicine reduced the cumulative incidence of delayed complications (1.58 % versus 8.4 %, p<0.01). Follow-up TEE showed a leak of 2–5 mm in 6.5% and a thrombus in 2.5%. One patient had a leak of >5 mm. Several other studies have demonstrated >92% success rates with a low rate of complications. Bartus et al. showed that 85 out of 89 patients (96%) underwent successful LAA ligation. There were three access related complications due to pericardial access (n=2) and transseptal catheterization (n=1). Other adverse events included severe postoperative pericarditis (n=2), late pericardial effusion (n=1), unexplained sudden death (n=2), and late strokes (n=2). Stone et al. showed that out of 27 patients, one patient had LAA perforation. Peri-operative complications include two pericarditis, one stroke, and one pleural effusion. Massumi et al. showed that all 21 patients had successful LAA exclusion. One patient had cardiac perforation and tamponade that required cardiac surgery. Three patients developed pericarditis; one had pericardial effusion that required drainage.

There is now early evidence that LAA exclusion and subsequent necrosis of the LAA leads to a reduction in AF burden in persistent AF patients. A multicenter randomized trial is ongoing to assess safety and effectiveness of the LARIAT® (SentreHEART, Inc.) system to percutaneously isolate and ligate the LAA. This will determine if LAA ligation as adjunctive therapy to pulmonary vein isolation (PVI) improves maintenance of sinus rhythm in patients with persistent and long-standing persistent AF.

Protean effects of LAA epicardial closure

LAA exclusion results in beneficial effects unrelated to stroke reduction. These effects were studied in depth in patients undergoing the LARIAT® (SentreHEART, Inc.)
closure. A brief summary of these effects is described below.

**Antihypertensive effect of LAA exclusion**

LAA exclusion through surgical excision or LARIAT\(^{(R)}\) (SentreHEART, Inc.) procedure influences neurohormonal function resulting in reduction of renin, aldosterone, and noradrenaline levels, which translate to a lower systolic blood pressure.\(^{50}\) Maybrook et al.\(^{53}\) evaluated the electrolytes and hemodynamic changes after the LARIAT\(^{(R)}\) (SentreHEART, Inc.) procedure. There was a significant reduction in systolic blood pressure at 24 hours (113.3 ± 16.0; \(p < 0.0001\)) and 72 hours (119.0 ± 18.4 mmHg; \(p < 0.0001\)) compared with baseline systolic blood pressure prior to the LARIAT\(^{(R)}\) (SentreHEART, Inc.) procedure (138.2 ± 21.3).\(^{53}\) This is clearly better than the 6 mmHg reduction in blood pressure shown after renal denervation therapy.\(^{54}\)

**LARIAT\(^{(R)}\) as an adjunctive for rhythm control during AF ablation**

The LAA appendage is a possible source of the trigger for AF in patients with non-paroxysmal AF. Although ablation of the LAA to achieve electrical isolation is possible, electrical isolation of the LAA during catheter ablation can be challenging and may potentially result in thrombus formation in the LAA.\(^{55}\) Occlusion of the LAA leads to necrosis and ultimately renders the LAA electrically non-viable. One study of 69 patients with LAA ligation followed by ablation at least 30 days after the procedure showed higher AF freedom when off antiarrhythmic drugs in the LARIAT\(^{(R)}\) (SentreHEART, Inc.) plus ablation group versus ablation-only group 65% versus 39% (\(P = 0.002\)).\(^{26}\) Similar studies have shown reduction of AF burden post LARIAT\(^{(R)}\) (SentreHEART, Inc.).\(^{56}\) There is currently an ongoing randomized trial to obtain more evidence in this regard.\(^{52,56}\) Although endocardial devices such as the WATCHMAN™ (Boston Scientific) achieve mechanical exclusion of the LAA, they do not ultimately achieve electrical occlusion. LAA exclusion via the epicardial approach has been shown to result in a permanent transmural lesion, achieving both mechanical and electrical isolation of the LAA.\(^{46-48,57}\)

**Neurohormonal effects of LAA occlusion**

LAA exclusion with an epicardial system (Lariat\(^{(R)}\), Sentreheart, Inc.) has been shown to have neuroendocrine sequelae such as a decrease in norepinephrine and atrial natriuretic peptide (ANP) levels.\(^{53}\) The clinical significance is currently unknown and more research is needed to elucidate the clinical benefits of such neurohormonal changes post LAA occlusion.

From the above-mentioned data, it is clear that LAA exclusion is both a feasible and an effective procedure and offers an attractive alternative to AC, especially in patients who are deemed to be high-risk candidates for long-term AC. With spiraling healthcare expenditures, one then wonders if LAA exclusion is feasible economically. The following analyses address this question.

**Cost effectiveness of left atrial appendage closure**

Some studies have suggested that LAA closure is cost effective in the long run. LAA closure is associated with an upfront procedural cost that is offset later due to the absence of the cost of oral AC therapy and associated complications.\(^{12}\) Recently, Panikker et al.\(^{58}\) published a cost–impact analysis from randomized clinical trial studies and real-world experience comparing the cost of LAA closure using the WATCHMAN™ (Boston Scientific) with available oral anticoagulants. The study showed that LAA closure with the WATCHMAN™ (Boston Scientific) in a real-world setting may result in lower stroke and major bleeding rates than that reported in clinical trials.\(^{59}\) The cost of LAA closure achieved cost parity in a relatively short period of time. This would offer substantial cost savings compared with long-term oral AC (Figure 1).\(^{58}\) This cost effectiveness of the WATCHMAN™ (Boston Scientific) device is most pronounced in patients at high thromboembolic risk who are not suitable for long-term AC.\(^{58}\) Saw et al.\(^{59}\) evaluated the cost effectiveness of ACP comparison with aspirin alone. In this study, ACP was found to be more effective and less expensive than aspirin. The average discounted lifetime cost was $30,830 ± $11,726 for ACP and $39,751 ± 18,943 for aspirin.\(^{59}\) Reddy et al.\(^{13}\) studied the cost effectiveness of the WATCHMAN™ (Boston Scientific) device compared with apixaban in patients with non-valvular AF and contraindications to warfarin. In this study, the WATCHMAN™ (Boston Scientific) was cost-effective at 5 years compared with aspirin. It was more cost effective than apixaban after 7 years, and it was more cost effective than apixaban and aspirin after 8 years.\(^{13}\) This study used a cost-effectiveness model that uses one metric to account for cost, clinical effectiveness, and patient outcomes. The risk and cost of stroke as well as quality of life and functional outcomes after stroke were also studied. Strokes occurring in patients following left atrial appendage closure (LAAC) procedures were less disabling. The MRS (modified Rankin score) in patients who had the WATCHMAN™ (Boston Scientific) was 0–2 in 24% of the warfarin group versus 44% in the NOAC group. This suggests that most LAAC-treated patients with stroke return to baseline daily activity without a major hurdle following a stroke.\(^{13}\) Another study by Reddy et al.\(^{12}\) studied the cost-effectiveness analysis comparing warfarin, NOACs, and the WATCHMAN™ (Boston Scientific) procedure in patients with non-valvular atrial fibrillation (NVAF). The study showed that both NOACs and WATCHMAN™ (Boston Scientific) were cost effective compared with warfarin, but the WATCHMAN™ (Boston Scientific) group was found to be more cost effective than the NOAC group.
Figure 2. These studies show the cost effectiveness of the LAAC device for Watchman™ (Boston Scientific) and ACP. A similar analysis for the LARIAT® (SentreHEART, Inc.) device has not yet been done.

Conclusion

Stroke prophylaxis is the central goal in patients with AF. The strategy of pharmaco-prophylaxis is associated with several challenges. The LAA exclusion strategies have a favorable outcome in several randomized and non-randomized studies. The only FDA-approved device is the WATCHMAN™ (Boston Scientific); however, it is not recommended for AC-ineligible patients yet. Although there is no randomized controlled trial, LARIAT® (SentreHEART, Inc.) has been used in >4,000 patients and shown to be efficacious and safe by and large. It is also associated with beneficial adjunctive effects such as reduction of AF burden and improved blood pressure control. It does not require peri-procedural AC and thus is probably the best available option for AC-ineligible patients who are not ideal candidates for surgical techniques. In this regard, it has a special niche in terms of stroke prevention. Although the data on the LAA occlusion device are promising, it is important to note that none of the LAA occlusion devices have been compared head to head with long-term NOACs. Therefore, until more data are available, the LAA occlusion devices should not be considered as a substitute for oral AC. The use of left atrial occlusion devices should be carefully evaluated and reserved for selected patients who are at the highest risk of stroke and bleeding who cannot tolerate oral AC. Appropriate device and patient selection is crucial. With increasing operator experience and safer pericardial access techniques, LAA exclusion devices have been shown to be safe, effective, and likely reduce overall health care cost associated with stroke prevention in the long run.
References


50. Lakkireddy D. Left atrial appendage exclusion as adjunct strategy for AF ablation. Paper presented at: 35th Annual Meeting of the Heart Rhythm Society; May 7–10, 2014; San Francisco, CA.


