Left Atrial Appendage Closure Devices

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ABSTRACT: Atrial fibrillation (AF) increases the risk for thromboembolic stroke five-fold. The left atrial appendage (LAA) has been shown to be the main source of thrombus formation in the majority of strokes associated with AF. Oral anticoagulation with warfarin and novel anticoagulants remains the standard of care; however, it has several limitations, including bleeding and poor compliance. Occlusion of the LAA has been shown to be an alternative therapeutic approach to drug therapy. The purpose of this article is to review the different techniques and devices that have emerged for the purpose of occluding this structure, with a particular emphasis on the efficacy and safety studies published to date in the medical literature.

KEYWORDS: Atrial appendage, Atrial fibrillation, LAA, Atrium closure devices

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Introduction

One of the most common arrhythmias is atrial fibrillation (AF), which affects approximately 2% of the population worldwide. The prevalence of AF is predicted to increase five-fold over the next 40 years, particularly in the United States, primarily due to the growing elderly population. AF is a global epidemic condition that has a known significant impact on health care costs and progressive effects on estimates of disability and mortality. From 1990 to 2010, there was an 18% increase in disability-adjusted life years. Furthermore, the age-adjusted mortality rate increased two-fold in males and 1.9-fold in females in 2010. AF is associated with significant morbidity and mortality, including stroke, heart failure, and death. The most feared complication of AF is a thromboembolic episode that causes a cerebrovascular accident (CVA). The risks of thromboembolic complications and stroke remain the same regardless of whether a person has paroxysmal, persistent, or long-standing persistent AF. Moreover, AF increases the risk of stroke five-fold, and 15–20% of all strokes are attributable to this condition.

There are two primary methods of preventing stroke in patients with AF, namely, oral anticoagulation (AC) therapy, and left atrial appendage (LAA) occlusion or removal. AC therapy is the mainstay of medical therapy for AF. Nevertheless, a significant number of patients have relative or absolute contraindications to AC therapy. Similarly, approximately 50% of patients on warfarin sodium (Coumadin) are within the therapeutic range, and the overall withdrawal rate after one year is 10–38%. Warfarin is associated with bleeding, difficult monitoring, narrow therapeutic windows, and multiple drug interactions. Novel oral anticoagulant agents, such as apixaban (Eliquis™), dabigatran (Pradaxa™), and rivaroxaban (Xarelto™), have been demonstrated to be non-inferior/superior to warfarin. Novel oral anticoagulants are associated with bleeding complications, drug interactions, and increased costs. These factors have led investigators to seek alternative therapeutic strategies to prevent CVA in patients with AF.

Compelling evidence has revealed that the LAA is the most common anatomical site for thrombus formation in patients with AF. Approximately 90% of all clots in non-valvular AF are localized to this structure. Therefore, patients with contraindications for AC therapy and who have a high risk of life-threatening bleeding while taking anticoagulant therapy may benefit from LAA occlusion. Non-surgical approaches to LAA occlusion have been developed and are the main focus of this review.
In 1949, Madden performed the first LAA excision in two patients with AF and rheumatic mitral disease. In another study, the prophylactic removal of the LAA in patients with AF undergoing open-heart surgery resulted in the complete elimination of post-procedure atrial clots, resulting in the conclusion that LAA removal should be considered during open-heart surgery.10 The left atrial appendage occlusion study (LAAOS) was the first randomized trial to evaluate the safety and efficacy of LAA occlusion at the time of elective bypass graft surgery.11 The LAOOS included 77 patients with a high risk of stroke (11 with a history of AF), and LAA occlusion was attempted using sutures and staples. Occlusion was achieved in only 66% of the patients, with the use of staples demonstrating the highest efficacy. The efficacy was assessed with transesophageal echocardiography (TEE) at eight weeks, revealing efficacies of staples and sutures of 72 and 45%, respectively.11

Similarly, a meta-analysis of five clinical trials demonstrated a limitation of the surgical approach due to incomplete exclusion of the LAA. The study included 1400 patients and concluded that there was no clear benefit from LAA surgical exclusion. Only one of the five studies demonstrated benefits; another study revealed increased risk, and the remaining three studies revealed neither risks nor benefits associated with this technique.12

LAA exclusion has long been pursued surgically, and more recently, has been pursued using implantable devices. The main limitation of the surgical approach is incomplete exclusion, which is as high as 40% (successful LAA closure occurred more frequently with excision (73%) than with suture or staple exclusion (23%)).13

**Left Atrial Closure Devices**

Occluding the LAA has been shown to reduce the risk of stroke in AF patients.14 A decade ago, the first study in which closure devices were percutaneously implanted in humans, called the LAPTONI procedure, was published.15 Thereafter, several devices were proposed and tested for efficacy and safety. Among these devices, the most studied include the PLAATO system (ev3 Endovascular, Plymouth, MN), the WATCHMAN device (Boston Scientific, Plymouth, MN), the Amplatzer Cardiac Plug (ACP, St. Jude, Golden Valley, MN), and the LARIAT device (SentreHEART, Palo Alto, CA). These devices were generally implanted by endovascular techniques (with the exception of the LARIAT device, which also required epicardial access), which only required a minimal skin incision. The devices were delivered via percutaneous 9-Fr to 14-Fr catheters from the femoral vein to the LAA via transseptal puncture.16

These endovascular techniques have been investigated, and the percentage of closure depends on the employed modality and the LAA anatomy. Consequently, cardiac imaging has become of paramount importance for LAA anatomical characterization and device placement.17 Measurements of the LAA orifice diameters are increasingly essential to ensure the correct sizing and deployment of the occlusion device to optimize effectiveness and minimize complications.18 The best imaging modalities for performing this measurement are cardiac computed tomography (CCT),19 cardiac magnetic resonance (CMR),20 and 3-D TEE,21 which, as expected, provides more precise values than 2-D TEE.22 It is worth mentioning that measuring LAA length and LAA ostium diameter by 2-D TEE23 clearly underestimates dimensions,
as demonstrated by the CUTE-CV study, in which a contrast agent was utilized. Accordingly, Definity or Optison contrast agents should be used to obtain more accurate measurements when 2-D TEE is used for this purpose.\(^{24}\) Finally, TEE or intracardiac echocardiography (ICE) is routinely used to ensure the absence of LAA thrombus and to obtain left atrial (LA) access through a transseptal puncture.\(^{25}\) Once the device is in the left atrium, TEE, ICE, and/or fluoroscopy guidance are necessary to position the device in the LAA.

The LAA is composed of two lobes in half of the population and three lobes in one-third of the population.\(^{26}\) Several LAA morphologies (Fig. 1) have been described; however, the four most common and clinically used morphologies are the chicken wing (48%), cactus (30%), windsock (19%), and cauliflower (3%). Di Biase et al demonstrated that LAA morphology correlates with the risk of stroke in patients with AF.\(^{27}\) In this study, patients with the chicken wing morphology were less likely to have CVAs compared with patients with the other three morphologies (4 vs. 10–18%).\(^{27}\) The morphology of the LAA was shown to be predictive of the risk of stroke/transient ischemic attack (TIA) and may be considered when planning AC therapy in patients with AF.

One of the main indications for LAA closure devices in patients with AF is an absolute contraindication to long-term AC therapy. Other indications are a high risk of bleeding with AC therapy and a high risk of stroke with relative contraindications to AC therapy.

**PLAATO.** PLAATO (ev3 endovascular, Plymouth, MN), reported in 2002, was the first approved device for LAA closure.\(^{28}\) The device consists of a self-expanding nitinol cage covered with polytetrafluoroethylene. Three rows of anchors along the maximum circumference secure the cage within the LAA ostium. Although it produced positive five-year study results, the device was discontinued in 2007\(^{29}\) for commercial reasons.\(^{29,33}\) The PLAATO device diameters ranged from 15–32 mm and were selected such that they were 20–40% larger than the LAA ostium diameter (Fig. 2).\(^{30}\)

Two prospective multicenter trials have evaluated the efficacy of the PLAATO system. In the international multicenter feasibility trial, the PLAATO system was used in 111 patients with non-valvular AF with contraindications to AC therapy. Occlusion was achieved in 97.3% of the patients (95% confidence interval [CI] 92.3–99.4%). The primary endpoint was the incidence of major adverse events (MAEs).\(^{31}\) There were seven MAEs: two strokes, four cardiovascular or neurological deaths, and one cardiovascular surgery requirement (after the device implantation and within 30 days after the procedure).\(^{31}\) Three TIAs occurred in the five-year follow-up period.\(^{32}\) The annualized stroke or TIA rate using the PLAATO system was 3.8% (3.2% for a similar cohort taking Coumadin from the PROTECT AF trial), compared with an expected 6.6% stroke rate using the CHADS2 scoring system (mean score of 2.6).\(^{14,16}\) The European PLAATO study enrolled 180 patients with non-valvular AF and contraindications to warfarin. LAA closure confirmed by TEE two months after the procedure was the primary endpoint. Complete occlusion was achieved in 90% of the patients. There were two severe adverse events, including two procedure-related deaths.\(^{33}\) The annualized stroke rate with the PLAATO system was estimated to be 2.3%, and the expected incidence of stroke according to the CHADS2 score was 6.6%.\(^{16}\)

One study examined the utility of ICE for providing guidance as an alternative to TEE during PLAATO system implantation. The study concluded that ICE (1) provided

![Figure 1](image1.png)  
**Figure 1.** LAA morphologies. The four most common LAA morphologies are shown on the left side of the cardiac CT images and are shown on the right side of the cardiac MRI images: (A) cactus, (B) windsock, (C) cauliflower, and (D) chicken wing. This image was published in Di Biase L, et al. Does the left atrial appendage morphology correlate with the risk of stroke in patients with atrial fibrillation? Results from a multicenter study. JACC. 2012;60(6):531–8. Copyright Elsevier 2012.

![Figure 2](image2.png)  
**Figure 2.** PLAATO device. The device consists of a nitinol cage covered with polytetrafluoroethylene; note how the device occludes the LAA ostium.
high-resolution images to enable assessment of proper positioning and exclusion of thrombus and (2) decreased overall cost by obviating the need for a second physician during the intervention. A disadvantage of ICE may be the inability to acquire 3-D images.25

Watchman. The Watchman device (Atritech, Inc., Boston Scientific, Plymouth, MA) is the only LAA occlusion device currently being considered for full US FDA approval.14 The device has a self-expanding nitinol frame with fixation barbs and a permeable polyester fabric cover (Fig. 3).

The device is available in five different sizes, namely, 21, 24, 27, 30, and 33 mm in diameter and height. Appropriate sizing requires the device to be approximately 10–20% larger than the LAA.35 To implant the Watchman device, a specialized 12-F access sheath is used to enter the LAA and serves as a duct for the delivery catheter. After access is obtained under TEE and fluoroscopy guidance, a pigtail catheter is advanced into the LAA, and the sheath is then advanced over the pigtail into the LAA. The pigtail catheter decreases the probability of LAA perforation. The preloaded delivery catheter is advanced into the tip of the access sheath and is deployed by a gentle retraction of the sheath.35

The first Watchman study was an open-label nonrandomized pilot study.36 Sixty-six patients with non-valvular AF were included. At 45 days, 93% of the devices properly sealed the LAA. The primary endpoint was successful implantation and sealing of the LAA, confirmed by TEE. The first-generation device yielded two device embolizations and one delivery system failure. The device was redesigned (modified fixation barbs) after implantation of the first 16 patients. Subsequent patients (53) underwent implantation with the second-generation device. In this study cohort, the expected annual risk of stroke based on the CHADS2 score was 1.9/year and was 3.2% for a similar cohort taking warfarin14; however, none of the patients experienced a stroke in the two-year follow-up period.6,36

The PROTECT AF study was a multicenter randomized trial that assessed the non-inferiority of the Watchman device to AC therapy in patients with non-valvular AF.34,37 Efficacy was assessed by a primary composite endpoint of systemic embolism, cardiovascular death, and stroke. After the Watchman device was implanted, warfarin administration was followed for 45 days until endothelialization was achieved.38 TEE was performed at 45 days, 6 months, and 12 months. The warfarin was discontinued after 45 days, and the patients were prescribed clopidogrel 75 mg daily for six months, followed by aspirin 81–325 mg for life.39 A total of 408 patients underwent device implantation, and 241 received warfarin. The device implantation was successful in 91% of the patients. The control group had a higher prevalence of major bleeding (4.1%) compared with the device group (3.5%). The device group had a higher ischemic stroke risk (2.2%) based on CHADS2 score compared with the control group (1.6%), but hemorrhagic strokes were less frequent in the intervention group (0.2%) than in the control group (2.5%). Device embolization took place in 0.6%. The rate of all hemorrhagic and ischemic strokes was lower in the intervention group than in the control group. The PROTECT AF study showed that closure of the LAA was not inferior to chronic warfarin therapy.14

The Continued Access Registry trial was a cohort study that included patients from the PROTECT AF trial (542 patients) and patients undergoing Watchman implantation (continued access protocol, 460 patients). The patients were followed for a median of 2.5 years. The trial demonstrated a significant improvement in the safety of the Watchman device with increased operator experience.39

In the PREVAIL study (Please note this study has not been published in a peer-reviewed journal), patients with a CHADS2 score of 1 were excluded. A total of 407 patients were included in a randomized trial similar to PROTECT AF. The adverse event rate in the first seven days was lower than that in a previous study (2.2 vs. 2.67% based on pre-specified criteria).40 The implantation success rate increased similarly to that of PROTECT AF (90.9 vs. 95.1%). The safety endpoint (seven-day occurrence of death, ischemic stroke, procedure-related complications requiring intervention, and systemic embolism) was also reduced by 2.61% compared with the pre-specified criterion of 2.67%. The PREVAIL control group demonstrated a lower rate of stroke (0.7%) than is typically found in studies of patients taking warfarin (1.6–2.2%).4,14 Complications associated with device implantation were significantly lower than those in previous studies, confirming the acute procedure- and device-related safety of this technique.34,40 Conversely, the second co-primary endpoint which was a composite of stroke, systemic embolism, and cardiovascular or unexplained death at 18 months was not met. The observed adverse event rate for both the WATCHMAN group and the warfarin group were 0.064, resulting in a RR of 1.07 with an observed upper bound of 1.88, slightly greater than the pre-specified criterion of 1.75 (95% CI).

LARIAT. The LARIAT (SentreHEART, Palo Alto, CA, USA) system device consists of three components: (1) a balloon catheter (EndoCATH 15 mm), (2) magnet-tipped

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Figure 3. WATCHMAN device. This parachute-shaped device consists of a nitinol cage with a polytetrafluoroethylene membrane and includes a row of fixation barbs.
guidewires (FindrWIRZ 0.025–0.035 inches), and (3) an epicardially delivered 12-F suture delivery device (LARIAT).""}

The LARIAT system device requires both epicardial and endocardial approaches to occlude the LAA. Four steps are required: (1) accessing the pericardial and transseptal spaces, (2) placing the endocardial magnet-tipped guidewire in the apex of the LAA with balloon identification of the LAA, (3) connection of the epicardial and endocardial magnet-tipped guidewires for stabilization of the LAA, and (4) snare capture of the LAA with closure confirmation and release of the pretied suture for LAA ligation (Fig. 4).""

As the LAA is closed from the outside with a single ligature, there is no permanent intracardiac foreign body left behind and no risk of device embolization. Owing to its lack of endovascular hardware, patients with an increased risk of infection may benefit from the use of this system. Patients being considered for epicardial ligation of the LAA using the LARIAT device must undergo a CT scan of the heart with contrast to ensure that the size and orientation of the appendage are amenable to ligation. Contraindications to this approach include an LAA width greater than 40 mm, a superiorly oriented LAA, and historical conditions that would result in pericardial adhesions. These conditions include a past history of pericarditis, open-heart surgery, epicardial ablation and thoracic radiation.

The initial LARIAT study was performed from February 2010 to February 2011 in 21 patients: 3 patients (14%) with paroxysmal AF, 11 patients (53%) with persistent AF, and 7 patients (33%) with persistent AF. The procedure was performed with TEE. The anterior pericardial space was accessed by an epidural needle, and a 14-Fr soft-tipped epicardial guide cannula was advanced over a 0.035-inch wire. An 8.5-Fr SL1 transseptal sheath was used to gain entry into the left atrium. The anatomy was visualized by angiography of the left atrium. The EndoCATH catheter has a balloon at its tip, and the balloon was inserted into the LAA through a guidewire (FindrWIRZ). An epicardial guidewire with a magnetic tip was inserted through the epicardial guide cannula into the pericardial space and was manipulated until it had attached to the endocardial magnetic tip. The LARIAT loop was positioned over the proximal part of the LAA after advancing it over the magnetic tip of the wire in the epicardium, guided by the balloon of the EndoCATH. The loop was closed after proper positioning, and closure was confirmed by the absence of flow in the LAA angiography and TEE (Fig. 5).

From the time of transseptal puncture until the time of transseptal sheath removal from the left atrium, the patients were anticoagulated with heparin boluses and infusions to achieve a target activated clotting time of >350 seconds. In most cases, heparinization was reversed with protamine at the end of the procedure. One patient experienced perforation...
of the right ventricle with tamponade, requiring surgical repair. Another patient required pericardiocentesis during the procedure to treat cardiac tamponade, and a third patient who experienced complications required prolonged intubation for chronic obstructive pulmonary disease (COPD) exacerbation and urosepsis. Three patients required hospitalization because they developed pericarditis. The LAA was occluded in 100% of patients. There were no strokes reported during the follow-up period (mean 352 ± 143 days; range 50–600 days). One patient died 50 days after surgery, but the death was thought to be unrelated to the procedure.

In another study, 27 patients with AF (14 with permanent, 11 with paroxysmal, and 2 with persistent AF), a CHADS2 score ≥2, and AC therapy contraindications or failure (from October 2011 to June 2012) were selected. LAA ligation was successful in 92.4% of patients, as confirmed by TEE. One patient sustained an LAA perforation, and in another patient, the investigators were unable to advance the LARIAT over the LAA. A 45-day follow-up TEE was performed and showed preserved LAA occlusion.

Manipulation of catheters in the pericardial space may produce inflammation and pericarditis. Patients often require anti-inflammatory therapy following this procedure. Based on two case reports, there is some concern regarding the capability of the epicardial suture snare to increase local inflammation and, therefore, thrombogenicity at the endocardial site in the left atrium, possibly requiring the use of anticoagulants after the procedure. Another theory is that by pulling the balloon-tipped catheter and endocardial magnet-tipped wire through a very narrow LAA neck the endothelium is traumatized creating a prothrombotic environment. Some patients may require AC; this need was demonstrated in two case reports in which, after a one-month follow-up, the patients showed partial reopening of the LAA with 2-D and 3-D echocardiography. Other complications of using LARIAT include LA laceration and cardiac tamponade.

ACP. The Amplatzer Cardiac Plug (ACP) (St. Jude) is a self-expanding device composed of nitinol wire mesh and polyester patch and consists of a lobe and a disk connected by a central waist. The lobe is shaped like a hockey puck and connects to a more proximal and larger disk with a small connecting waist. The lobe has diameters of 16–30 mm.

The device is usually selected to be 10–20% larger than the narrowest diameter of the LAA body. It was first designed for atrial septal defect closure. The device is delivered through a 10-F or 13-F sheath into the left atrium after transseptal puncture under real-time TEE and fluoroscopy. It is anchored in the LAA approximately 1 cm behind the ostium, and the disk is then unfolded to cover the entrance of the LAA. A safe placement is confirmed by a wiggle maneuver. A European study was conducted with 143 patients, with successful LAA closure achieved in 132 (96%) of patients. The mean age was 74 ± 9 years. Complications included pericardial effusion (five patients), ischemic stroke (three patients), and device embolization (two patients). In a second study performed by a single operator from June 2009 to March 2012, 100 patients underwent LAA closure with the ACP. Fifty-eight patients had permanent AF, 26 had paroxysmal AF, and 16 had persistent AF. The average age of the patients was 73 ± 9.9 years. Two complications were reported; one patient developed pericardial effusion with cardiac tamponade during the deployment of the device, and another patient developed respiratory distress with pulmonary edema.

A small study performed in Germany in 34 patients demonstrated thrombi formation using the ACP. These thrombi were noted on TEE in 17.6% of patients despite dual antiplatelet therapy. The majority of the thrombi formed on the central screw of the ACP. Investigators concluded that the device should be modified. The ACP has a larger surface area than the Watchman device, making it more prone to thrombi formation.

Consequently, a second-generation ACP, the AMULET device (St. Jude Medical, Saint Paul, MN, USA), was developed. This new device allows for larger LAA closure, improved stability and decreased embolization risk. The Amulet has a longer distal lobe length and a greater proximal disk diameter and waist than the ACP 1. The AMULET device, also called the ACP 2, is implanted in the same manner as the ACP 1 but is repositionable. Compared with the ACP 1, the ACP 2 has more hooks, which are also stiffer. It comes preloaded inside the delivery system and has a diameter of 16–34 mm. It is recommended that the device be selected such that it is approximately 3–6 mm larger than the LAA orifice.

L'Ambre. The L'Ambre is a self-expanding nitinol-based device consisting of a hook-embedded umbrella with a cover that is connected to a short central waist. The cover is larger than the umbrella by approximately 4–6 mm and is filled with sewn-in polyethylene terephthalate fabric (Fig. 7). The device comes in various sizes ranging from 16–36 mm.

When reaching the LAA through transseptal puncture using the conventional transseptal technique with an 8-Fr
transseptal sheath (SL1, St. Jude Medical), the LAA is accessed through a guidewire. After the transseptal puncture, a heparin bolus is administered. The size of the LAA is measured by angiography, and the size of the device is chosen such that it is 4–8 mm larger than the LAA. The delivery system is placed on the proximal part of the LAA, and the umbrella device is deployed by pushing the device out from the delivery sheath to the desired landing zone, opening the umbrella, and grasping the LAA walls with the hooks. The sheath is removed to expose the disk and to permit it to expand in the atrium and cover the LAA ostium by gently pushing the delivery cable forward. Placement is confirmed with LA angiography.\(^{57}\) This new device has two main advantages: a small delivery system and repositioning ability (during implantation).\(^{57}\)

**New LAA closure devices.** The AEGIS device permits LAA closure through an epicardial approach.\(^{58,59}\) This device has two parts: (1) appendage grabber and (2) ligator. The first component (grabber) has an articulating jaw with mounted electrodes, allowing the identification and positioning of the LAA by means of electrical signals. When positioning the electrodes near the LAA, the injection of contrast is used to outline the LAA and confirm proper capture by ICE or TEE. The ligator is a preloaded hollow suture that can be opened and closed repeatedly until proper closure has been achieved. This system has been tested in animals.

The Coherex WaveCrest (Salt Lake City, UT) is a device with an umbrella shape.\(^{60}\) It is deployed similarly to other endovascular devices and has been tested in animals and humans with satisfactory and promising results.

The Transcatheter Patch (Custom Medical Devices, Athens, Greece) is a soft, frameless, bioabsorbable balloon-deliverable device delivered similarly to other LAA occluders but is fixed within the LAA with a surgical adhesive (to reduce the risk of perforation). The supporting balloon and patch are composed of latex and polyurethane foam, respectively. The device was studied in 20 patients, revealing successful placement in 17 cases.\(^{61}\)

**Conclusion**

In patients with AF, stroke prevention is essential. Generally, oral AC is the mainstay therapy, but multiple adverse effects limit its use. LAA closure device studies have shown promising results, but until a large randomized clinical trial evaluating safety and long-term efficacy is performed, LAA occlusion should be considered only for individuals with a high risk of stroke and a high risk of bleeding while on anticoagulant therapy. The LARIAT device appears to be the safer device because it is deployed epicardially, with no risk of device embolization. Additionally, in most cases, this device does not require long-term AC, unlike other endovascularly deployed devices. However, a large randomized clinical trial is still needed.

**Author Contributions**

JR, IP, AK, MG, and RL conceived and designed this review article. JR and IP analyzed the data and reviewed the literature. IP and JR wrote the first draft of the manuscript. JR, IP, AK, MG, and RL contributed to the writing of the manuscript. JR, IP, AK, MG, and RL agree with manuscript results and conclusions. JR, IP, AK, MG, and RL jointly developed the structure and arguments for the paper. JR, IP, AK, MG, and RL made critical revisions and approved final version. All authors reviewed and approved of the final manuscript.

**DISCLOSURES AND ETHICS**

As a requirement of publication the authors have provided signed confirmation of their compliance with ethical and legal obligations including but not limited to compliance with ICMJE authorship and competing interests guidelines, that the article is neither under consideration for publication nor published elsewhere, of their compliance with legal and ethical guidelines concerning human and animal research participants (if applicable), and that permission has been obtained for reproduction of any copyrighted material. This article was subject to blind, independent, expert peer review. The reviewers reported no competing interests.

**REFERENCES**

1. Wilke T, Groth A, Mueller S, et al. Incidence and prevalence of atrial fibrillation: an analysis based on 8.3 million patients. Europace. 2013;15:486–93.
2. Chugh SS, Havmoeller R, Narayanan K, et al. Worldwide epidemiology of atrial fibrillation: a global burden of disease 2010 study. Circulation. 2013;129:837–47.
3. Camm AJ, Lip GY, De Caterina R, et al. 2012 focused update of the ESC Guidelines for the management of atrial fibrillation: an update of the 2010 ESC Guidelines for the management of atrial fibrillation—developed with the special contribution of the European Heart Rhythm Association. Europace. 2012;14:385–413.
4. Connolly SJ, Ezekowitz M, Yusuf S, et al. Dabigatran versus warfarin in patients with atrial fibrillation. N Engl J Med. 2009;361:1139–51.
5. Granger CB, Alexander JH, McMurray JJ, et al. Apixaban versus warfarin in patients with atrial fibrillation. N Engl J Med. 2011;365:981–92.
6. Patel M, Mahaffey K, Gang J, et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. N Engl J Med. 2011;365:883–91.
7. Marjoni E, Le Heuzey JY, Connolly S, et al. Causes of death and influencing factors in patients with atrial fibrillation: a competing risk analysis from the randomized evaluation of long-term anticoagulant therapy study. Circulation. 2013;128:2192–201.
8. Alli O, Holmes DR Jr. Left atrial appendage occlusion for stroke prevention. Curr Probl Cardiol. 2012;37:405–41.
9. Canestaro WF, Patrick AR, Avorn J, et al. Cost-effectiveness of oral anticoagulants for treatment of atrial fibrillation. Circ Cardiovasc Qual Outcomes. 2013;6:724–31.
33. Bayard YL, Omran H, Neuzil P, et al. PLAATO (Percutaneous Left Atrial Appendage Occlusion) trial. J Am Coll Cardiol. 2006;47:43–51.

34. Block PC, Burstein S, Casale PN, et al. Percutaneous left atrial appendage occlusion for stroke prevention in non-paroxysmal atrial fibrillation: a randomized controlled trial. J Am Coll Cardiol. 2004;43:426–31.

35. Nakamura M, Kar S. Transcatheter occlusion of the left atrial appendage. Intervent Cardiol Clin. 2013;2:225–34.

36. Sick PB, Schulter G, Hauptmann KE, et al. Initial worldwide experience with the WATCHMAN left atrial appendage system for stroke prevention in atrial fibrillation. J Am Coll Cardiol. 2007;49:1490–6.

37. Fontaine RB, Holmes DR, Chandrasekaran K, et al. The PROTECT AF (WATCHMAN Left Atrial Appendage System for Embolic Protection in Patients with Atrial Fibrillation) trial. Am Heart J. 2006;151:956–61.

38. Reddy VY, Doshi SK, Siever H, et al. Percutaneous left atrial appendage closure for stroke prophylaxis in patients with atrial fibrillation: a randomized, non-inferiority trial. J Am Coll Cardiol. 2009;54:42–52.

39. Blackshear JL, Johnson WD, Odell JA, et al. Thoracoscopic extracardiac obliteration of the left atrial appendage for stroke risk reduction in atrial fibrillation. J Am Coll Cardiol. 2003;42:1249–52.

40. Don CW, Fuller CJ, Reisman M. Transcatheter left atrial appendage occlusion. Circulation. 2013;127:720–9.

41. Werner CA, Cifaldi MP, Pettersson GB, Blackstone E, Klein AL. Success of surgical left atrial appendage closure: assessment by transeosophageal echocardiography. J Am Coll Cardiol. 2008;52:924–9.

42. Holmes DR, Reddy VY, Turi ZG, et al. Percutaneous closure of the left atrial appendage versus warfarin therapy for prevention of stroke in patients with atrial fibrillation: a randomized, non-inferiority trial. J Am Coll Cardiol. 2009;54:42–52.

43. Stone D, Byrne T, Perchad 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 [Epub ahead of print].

44. Patel TK, Yancy CW, Knight BP. Left atrial appendage exclusion for stroke prevention in atrial fibrillation: two patient cohorts. J Am Coll Cardiol. 2013;62:108–18.

45. Mozes WJ, Smith MR, Price PJ. Percutaneous management of late leak after lariat transcatheter ligation of the left atrial appendage in patients with atrial fibrillation at high risk for stroke. Circulation. 2013;111:869–73.

46. Giedreimas E, Lin AC, Knight BP. Left atrial thrombus after appendage closure using the LARIAT device. Circ Arrhythm Electrophysiol. 2013;6:52–3.

47. Bocchi F, Perri F, Turi ZG, et al. Early experience with the Amplatz Cardiac Plug after left atrial appendage exclusion device in patients with atrial fibrillation. Heart. 2013;99:73–82.

48. Healey JS, Crystal E, Lamy A, et al. Left Atrial Appendage Occlusion Study (LAOOS): results of a randomized controlled pilot study of left atrial appendage occlusion during coronary bypass surgery in patients at risk for stroke. Am Heart J. 2002;155:285–92.

49. Dawson AG, Asopa S, Dunnin J. Should patients undergoing cardiac surgery with atrial fibrillation have left atrial appendage exclusion? Interact Cardiovasc Thorac Surg. 2010;10:306–11.

50. Ostermayer SH, Reisman M, Kramer PH, et al. Percutaneous left atrial appendage closure: preliminary results of an early reopening of the LARIAT epicardial left atrial appendage closure device. Heart. 2013 [Epub ahead of print].

51. Keating VP, Kolibash CP, Khandheria BK, Bajwa T, Se A, Kress DC. Left atrial laceration with epicardial ligation device. Ann Thorac Cardiovasc Surg. 2013;19:106–13.

52. Lam YY, Yip GW, Yu CM. Left atrial appendage closure with AMPLATZER cardiac plug for stroke prevention in atrial fibrillation: initial clinical experience. Jpn J Thorac Cardiovasc Surg. 2012;70:79–84.

53. Meekin DK, Buttner A, Dratva D, Berendt OF, Trivoni D. Early safety of the Amplatzer Cardiac Plug for left atrial appendage exclusion. J Cardiovasc Electrophysiol. 2013;24:961–9.

54. Park JW, Bethencourt A, Sievert H, et al. Left atrial appendage closure: preliminary report of the WATCHMAN Left Atrial Appendage System for Embolic Protection in Patients with Atrial Fibrillation trial. Circulation. 2013;127:720–9.

55. Reddy VY, Holmes D, Doshi SK, Neuzil P, Kar S. Safety of percutaneous left atrial appendage closure: results from the Watchman Left Atrial Appendage System for Embolic Protection in Patients with AF (PROTECT AF) clinical trial and the Continued Access Registry. Circulation. 2011;123:47–24.

56. Boston Scientific. PREVAIL Study: prospective randomized evaluation of the WATCHMAN LAA device closure in patients with atrial fibrillation versus long term warfarin therapy. 2013. Available at http://www.bostonscientific.com/Watchman-clinical-data/prevail-clinical-study.html.

57. Bartus K, Bednarzek J, Myc J, et al. Feasibility of closed-chest ligation of the left atrial appendage in humans. Heart. 2011;88:158–36.

58. Bartus K, Han FT, Bednarzek J, et al. Percutaneous left atrial appendage suture ligation using the LARIAT device in patients with atrial fibrillation: initial clinical experience. J Am Coll Cardiol. 2013;62:108–18.

59. Brotman AM, Lahiri P, Rezende PH, et al. Analysis of the left atrial appendage by three-dimensional transesophageal echocardiography. J Cardiovasc Electrophysiol. 2010;21:973–82.

60. Nakajima H, Seo Y, Ishizu T, et al. Analysis of the left atrial appendage by three-dimensional transesophageal echocardiography. J Am Coll Cardiol. 2010;55:559–68.

61. Yokoyama A, Sogawa S, Takeda K, et al. Morphological features of the left atrial appendage in patients with atrial fibrillation: a quantitative study obtained by pre-procedural cardiac computed tomography and trans-thoracic echocardiography. Int J Cardiovasc Imaging. 2013;29:1423–32.

62. Arkwright DE, Dorey FM, et al. Images in cardiology. Computed tomography in atrial fibrillation. Heart. 2006;92:486.

63. Heist EK, Reisfai M, Danik SB, Holmang V, Ruskin JN, Mansour M. Analysis of the left atrial appendage by magnetic resonance angiography in patients with atrial fibrillation. Heart. 2006;92:1313–18.

64. Wang Y, Di Biase L, Horton RP, Nguyen T, Morhanty P, Natale A. Left atrial appendage thrombus: use of intracardiac echocardiography to guide device placement. J Am Heart Assoc. 2013;2:1–8.

65. Healey JS, Crystal E, Lamy A, et al. Left atrial appendage exclusion device in patients with atrial fibrillation, increased stroke risk, and contraindications to anticoagulation. Am J Cardiol. 2013;111:869–73.

66. Healy JS, Crystal E, Lamy A, et al. Images in cardiology. Computed tomography in atrial fibrillation. Heart. 2006;92:486.

67. Healey JS, Crystal E, Lamy A, et al. Images in cardiology. Computed tomography in atrial fibrillation. Heart. 2006;92:486.

68. Healey JS, Crystal E, Lamy A, et al. Images in cardiology. Computed tomography in atrial fibrillation. Heart. 2006;92:486.

69. Healey JS, Crystal E, Lamy A, et al. Images in cardiology. Computed tomography in atrial fibrillation. Heart. 2006;92:486.

70. Healey JS, Crystal E, Lamy A, et al. Images in cardiology. Computed tomography in atrial fibrillation. Heart. 2006;92:486.

71. Healey JS, Crystal E, Lamy A, et al. Images in cardiology. Computed tomography in atrial fibrillation. Heart. 2006;92:486.

72. Healey JS, Crystal E, Lamy A, et al. Images in cardiology. Computed tomography in atrial fibrillation. Heart. 2006;92:486.

73. Healey JS, Crystal E, Lamy A, et al. Images in cardiology. Computed tomography in atrial fibrillation. Heart. 2006;92:486.