CONTEMPORARY REVIEW

Left atrial appendage closure: A new technique for clinical practice

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BACKGROUND/OBJECTIVE Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia. It is associated with increased risk for stroke mainly due to cardiac embolism from the left atrial appendage (LAA). Occlusion of the LAA by means of a device represents a valid alternative to oral anticoagulation, mainly in patients who cannot tolerate this therapy because of a high bleeding risk. Recent data on the endocardial device WATCHMAN show encouraging results for this patient population in terms of stroke risk reduction compared to the expected rate as well as in terms of implant success. This article reviews all relevant publications related to the main surgical and transcatheter devices used for LAA closure (LAAC).

METHODS/RESULTS PROTECT-AF, the first prospective randomized trial conducted on this technique, showed that LAA occlusion using the WATCHMAN was noninferior to warfarin for a combined endpoint in patients with nonvalvular AF. There is a lack of large-scale randomized trials on long-term stroke risk in patients submitted to LAAC. Most studies are relatively small and focus on the comparison of different surgical techniques with regard to complete/incomplete closure success. More recently, PROTECT-AF long-term results (4-year follow-up) demonstrated that LAAC was statistically superior to warfarin in terms of efficacy.

CONCLUSION This review concludes that it is now appropriate to consider these techniques for patients with AF who are at high risk for stroke for whom effective conventional or novel anticoagulant therapy is not available or who present problems in managing drug treatment.

KEYWORDS Left atrial appendage; Left atrial appendage closure; Atrial fibrillation; Stroke risk; Thromboembolism

ABBREVIATIONS **ACP** = Amplatzer cardiac plug; **AF** = atrial fibrillation; **ESC** = European Society of Cardiology; **INR** = international normalized ratio; **LA** = left atrium; **LAA** = left atrial appendage; **LAAC** = left atrial appendage closure; **OAC** = oral anticoagulation; **TEE** = transesophageal echocardiography; **VKA** = vitamin K antagonism

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Introduction

Most strokes in patients with atrial fibrillation (AF) result from thrombus formation in the left atrial appendage (LAA). Beinart et al[1] and Thambidorai et al[2] found up to 90% of thrombi in the LAA in patients undergoing cardioversion.

The LAA lies anteriorly in the atrioventricular sulcus in close proximity to the left circumflex artery, the left phrenic nerve, and the left pulmonary veins. The shape of the LAA is variable; four main morphologies can be identified: "cactus," "chicken wing," "windsock," and "cauliflower." LAA morphology appears to be associated with different degrees of thromboembolic risk.[3] Patients with non–chicken wing LAA morphology are significantly more likely to have an embolic event, even after controlling for comorbidities and $CHADS_2$ score.[3,4]

In addition to LAA structure and function, the size of the left atrium (LA), left ventricular function, disorders of coagulation,[5,6] endothelial dysfunction, platelet activation,[7–10] and many comorbid conditions play a relevant role in stroke risk. Several scores have been developed and recommended in clinical practice to determine whether anticoagulation therapy should be prescribed for prevention of ischemic AF-related stroke.[11] $CHADS_2$ and CHA_2DS_2-VASc, the two most popular scores for assessing the risk of ischemic stroke, are recommended by guidelines; they take into consideration the comorbid conditions of the patient with AF.[12–14]

A large proportion of patients with indications for oral anticoagulation (OAC) either are never prescribed the therapy[15] or stop the treatment because of side effects, advice from their physicians, or their own decisions related to quality of life or bleeding concerns. In the RE-LY

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(Randomized Evaluation of Long-term anticoagulant therapy) trial, 10% and 17% of patients treated with warfarin stopped the treatment at 1 and 2 years, respectively.[16] Similarly, 15% and 16% of patients treated with dabigatran 110 mg stopped the treatment at 1 and 2 years, respectively (21% if considering dabigatran 150 mg).[16] In the ARISTOTLE (Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation) trial, 25% and 28% of patients discontinued apixaban and warfarin, respectively, during the trial.[17] Similarly, in the ROCKET-AF (Rivaroxaban Once daily oral direct factor Xa inhibition Compared with vitamin K antagonism [VKA] for prevention of stroke and Embolism Trial in AF) trial, 24% and 22% of patients stopped the treatment with rivaroxaban and warfarin, respectively, during the trial.[18] All patients who discontinue OAC are then treated with nothing or with antiplatelet therapy, unless the side effect is specific to a particular anticoagulant and therefore the patient becomes exposed to a high thromboembolic risk.

Warfarin and even more so the new OACs play a relevant role in reducing the thromboembolic risk associated with AF. On the other hand, inconsistent and inappropriate use, food–drug (VKA only) and drug–drug (VKA and novel OACs) interactions, and other side effects, particularly bleeding, must be considered when treatment based on anticoagulants is prescribed. Furthermore, as discussed earlier, some patients cannot be treated with anticoagulants because they have contraindications or are intolerant. Therefore, additional approaches to preventing AF-related stroke are needed.

Bleeding is also a clinically relevant adverse event in patients treated with antithrombotic therapy, and the physician must balance this risk with the risk of thromboembolism when deciding about OAC in patients with AF. The risk of bleeding can be determined using, for example, the HAS-BLED[19] or ATRIA[20] score. The 2012 update of the European Society of Cardiology (ESC) guidelines recommends using the HAS-BLED score to assess bleeding risk in AF patients, with a score ≥ 3 indicating high risk.

For all these reasons, surgical and transcatheter techniques have been explored to reduce the risk of stroke in persons with AF by excluding or occluding the LAA. Several methods can be used to close the appendage: direct suture during concomitant cardiac surgery, epicardial exclusion by stapling or clips, or endovascular occlusion by percutaneous application.

Nonpharmacologic treatments

The surgical approach

Amputation or obliteration of the LAA is considered in two possible situations: (1) as an additional procedure to either unrelated surgery or surgical MAZE procedures done specifically for management of AF, and (2) as an isolated closed chest (e.g., thoracoscopic) procedure.[21]

However, there is a lack of large-scale randomized trials on long-term stroke risk in patients submitted to surgical closure of the LAA. Most studies are relatively small and focus on the comparison of different surgical techniques with regard to complete/incomplete closure success. A larger randomized trial (Left Atrial Appendage Occlusion Study III [LAAOS III]) has been designed and is currently recruiting participants to evaluate the safety and efficacy of LAA removal in patients with AF undergoing heart surgery (Table 2).

Conclusions about stroke prevention by LAA exclusion or excision through surgery are still controversial.

The transcatheter approach

A technique that is intermediate between the surgical approach and the transcatheter approach is the endocardial/epicardial technique based on the LARIAT (SentreHEART Inc, Redwood City, CA) device.[22,23] The device is used for LAA ligation through a catheter (Figure 1D). Initial data on humans reported 96% implant success, and of the patients undergoing transesophageal echocardiography (TEE) at 1 year, there was 98% complete LAA closure (LAAC), including the patients with previous leaks.[22] Initial experience in the United States reported encouraging results in 25 patients, with 100% implant success and no strokes.[23]

To date, four devices with a purely endocardial approach have been investigated for LAA occlusion: the percutaneous LAA transcatheter occlusion (PLAATO) system (eV3, Plymouth, MN; Figure 1A), the Amplatzer cardiac plug (ACP) (St. Jude Medical, Minneapolis, MN; Figure 1B), the WATCHMAN device (Boston Scientific, Maple Grove, MN; (Figure 1C), and the Wavecrest System (Coherex Medical, Salt Lake City, UT; very little information available).[24]

All systems are delivered percutaneously through transseptal access to the LA.[24] Preprocedural evaluation of the LA and LAA, exclusion of thrombus, verification of placement, and evaluation of postprocedural pericardial effusion require skilled fluoroscopic and TEE coordination.[25] Cardiac magnetic resonance may offer some imaging advantages and help to select the type and size of device.[26,27] Computed tomography may also be a valid option to assist preoperative planning of LAA closure device placement.[28]

The PLAATO experience showed that, in a nonrandomized cohort, device implantation was feasible and safe, and, when compared with the historical stroke risk estimated using the $CHADS_2$ score, apparently cut the stroke rate by 40% to 65% in higher-risk AF patients. The PLAATO device has been discontinued for commercial reasons.

The ACP is a self-expanding device constructed from a nitinol mesh and polyester patch developed on the basis of Amplatzer double-disk septal occluders.[29] Patients implanted with this device are maintained on dual antiplatelet therapy with 1 to 3 months of clopidogrel followed by at least 5 months of aspirin. Limited data are available for the ACP, and the only randomized clinical trial that evaluated the device against optimal anticoagulation medical therapy (warfarin and dabigatran) is now underway.[30]