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REVIEW TOPIC OF THE WEEK

Strategies to Incorporate Left Atrial Appendage Occlusion Into Clinical Practice

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ABSTRACT

The left atrial appendage (LAA) has been identified as a predominant source of thrombus formation leading to significant thromboembolic events in patients with nonvalvular atrial fibrillation. Medical therapy to eliminate thrombus formation in the LAA has been the standard of care for several decades, but mechanical approaches designed to exclude the LAA from the circulation have recently been developed. The largest body of randomized and nonrandomized data to date has been for the Watchman device (Boston Scientific, Natick, Massachusetts), which was recently approved by the Food and Drug Administration for selected patients in the United States. There are no current guidelines or guidance for institutions and operators looking to become involved in this therapy. This perspective is aimed at exploring these issues and providing necessary information and guidance to these programs and operators to help ensure a successful launch of a LAA occlusion program and optimize patient selection, procedural performance, and outcome. (J Am Coll Cardiol 2015;65:2337–44) © 2015 by the American College of Cardiology Foundation.

Atrial fibrillation (AF) is a common arrhythmia encountered in clinical practice, with a prevalence of 2 million in the United States; this number is expected to increase to 16 million individuals by 2050 (1). A major consequence of AF is thromboembolism, particularly ischemic stroke; the risk of stroke in patients with AF is approximately 5% per year (2). Oral anticoagulation with warfarin and novel oral anticoagulant agents (NOACs) remain the cornerstone of stroke prevention in AF; warfarin has been shown to decrease the risk of stroke by as much as 65% (3), and the NOACs have similar efficacy with reduced risk of intracerebral hemorrhage.

Left atrial appendage (LAA) occlusion has emerged as a safe and effective alternative to the use of oral anticoagulation for stroke prevention in selected patients with nonvalvular AF (4–8). There are several devices currently in use for LAA occlusion, but the Watchman device (Boston Scientific, Natick, Massachusetts) has the most clinical trial data and is currently CE-marked and approved for use in Europe, with experience in approximately 50 countries. The U.S. Food and Drug Administration (FDA) recently approved the use of the Watchman device for reducing the risk of thromboembolism in patients with nonvalvular AF and increased risk of stroke where there is concern about the risks of long-term anticoagulant agents because of the risk of bleeding. At this time, institutions are beginning the process of designing and implementing clinical practice approaches for the introduction and use of these devices. This article aims to provide potential guidance for operators and institutions aiming to implement a LAA occlusion program.

From the *Division of Cardiovascular Diseases and Department of Internal Medicine, University of Alabama, Birmingham, Alabama; and the †Division of Cardiovascular Diseases and Department of Internal Medicine, Mayo Clinic and Mayo Foundation, Rochester, Minnesota. Dr. Alli has been a speaker for Edwards Lifesciences; and has received proctorship fees from Edwards Lifesciences. Dr. Asirvatham has received honoraria for consulting from Abiomed, Atricure, Biotronik, Biosense Webster, Boston Scientific, Medtronic, Spectranetics, St. Jude Medical, Sanofi, Wolters Kluwer, and Elsevier; and he is a co-holder of a patent and may receive future royalties from Aegis for appendage ligation. Dr. Holmes, along with Mayo Clinic, has a financial interest in technology that has been licensed to Boston Scientific. Ole De Backer, MD, PhD, served as Guest Editor for this paper.

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ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation

CT = computed tomography

DAPT = dual antiplatelet therapy

EP = electrophysiologist

FDA = U.S. Food and Drug Administration

IC = interventional cardiologist

ICE = intracardiac echocardiography

LAA = left atrial appendage

NOAC = novel oral anticoagulant agent(s)

OAC = oral anticoagulant agent(s)

TEE = transesophageal echocardiography

POTENTIAL OPPORTUNITIES AND BENEFITS OF LAA OCCLUSION

Although device-maker Boston Scientific highlighted the "first-of-its-kind alternative to long-term warfarin" (Coumadin) in announcing the approval of the LAA occlusion device (9), the indication was only for patients with nonvalvular AF who are at increased risk for stroke and systemic embolism on the basis of $CHADS_2$ (congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, prior stroke or TIA or thromboembolism) or CHA_2DS_2-VASc (congestive heart failure, hypertension, age ≤75 years, diabetes mellitus, prior stroke or TIA or thromboembolism, vascular disease, age 65 to 74 years, sex category) scores and deemed by their physicians to be suitable for warfarin, but who "have an appropriate rationale to seek a nonpharmacological alternative to warfarin" (10). Apart from this current indication, there are several other possible indications for use of this device:

Possible clinical scenarios (**Table 1**)

TABLE 1 Possible Clinical Scenarios for LAA Occlusion With the Watchman Device

1. As an alternative to oral anticoagulation in patients intolerant of OACs
2. Patients with high stroke and concomitant high bleeding risk
3. Patients with thromboembolic events while on OACs with therapeutic INR or on a NOAC and no other etiology for the clinical event
4. Patients that can tolerate oral anticoagulation and are also candidates for LAA device occlusion
5. Patients undergoing AF ablation or MitraClip implantation that may qualify for concomitant LAA occlusion at the same time of the original procedure

AF = atrial fibrillation; INR = international normalized ratio; LAA = left atrial appendage; NOAC = novel anticoagulant agent(s); OAC = oral anticoagulant agent.

1. As an alternative to oral anticoagulation in patients intolerant to oral anticoagulant agents (OACs). Current estimates suggest that up to 40% of people with AF and an indication for OAC have a relative or absolute contraindication to the use of warfarin, and <50% of eligible patients are being treated because of medication intolerance or noncompliance (10-13). Whether this pattern of underutilization will be similar with the several new OACs that are now approved is unknown. These agents have their own unique concerns, such as continued issues with gastrointestinal bleeding, cost, lack of antidotes, and for some of them, the need for twice-a-day dosing. Patients with previous intracranial bleeds, recurrent gastrointestinal bleeds, coagulopathies, and intolerance to NOACs/warfarin will still present clinical challenges. Unfortunately, there is a lack of randomized clinical trial data for use of the LAA occlusion device in these patients. The most robust data available for LAA device occlusion in this group comes from the European PLAATO (Percutaneous Left Atrial Appendage Transcatheter Occlusion) study (14) and the ASAP (Aspirin Plavix Feasibility Study with WATCHMAN Left Atrial Appendage Closure Technology) registry (15). In the ASAP registry, the predicted stroke rate depending on the $CHADS_2$ score was 7.3% per year and the observed stroke rate was 2.3%. It must be pointed out that these patients were on dual antiplatelet therapy (DAPT) for a duration of approximately 6 months and on aspirin indefinitely thereafter. Potential patients who would be enrolled into this pathway must be able to tolerate short-term DAPT and indefinite use of aspirin.
2. Patients with high stroke and concomitant high bleeding risk. A HAS-BLED (Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile INR [International Normalized Ratio], Elderly, Drugs/Alcohol Concomitantly) score ≥3 would suggest a high bleeding risk (16,17). In these cases, individual patient-level assessment is warranted to accurately quantify the stroke and bleeding risk; a trial of warfarin or NOACs may still be warranted, especially if the risk of intracranial hemorrhage is relatively low. Patients with high stroke risk, but unacceptable bleeding risk, should be considered for LAA device occlusion. Similarly, patients on triple anticoagulant therapy (DAPT and an OAC drug), such as those with atrial fibrillation who receive a drug-eluting stent, have an elevated bleeding risk; they may be considered for LAA device occlusion. Finally, patient subgroups with comorbidities associated with a high bleeding risk not captured by the HAS-BLED score, such as malignancy and inflammatory bowel disease, may also be considered for LAA device occlusion.
3. Patients with thromboembolic events while on OACs with therapeutic international normalized ratio or on a NOAC when no other etiology for the clinical event can be identified. In this group, LAA device occlusion may potentially be used as an adjunct to anticoagulation.
4. Patients that can tolerate oral anticoagulation and are also candidates for LAA device occlusion. This