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Case-Based Discussion Regarding Challenges in Patient Selection and Procedural Planning in Left Atrial Appendage Occlusion

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Abstract

Atrial fibrillation (AF) accounts for most embolic strokes, especially in elderly individuals. Although anticoagulation is known to reduce the risk of embolic stroke, a significant proportion of patients have relative or absolute contraindications to anticoagulation. The left atrial appendage has been implicated as the major source of emboli in more than 90% of ischemic strokes in nonvalvular AF. Left atrial appendage occlusion offers an alternative for stroke prevention in patients with an elevated stroke risk ($CHADS_2$ score $\geq$2 or CHA_2DS_2-VASc score $\geq$3) who have a rationale for avoiding long-term oral anticoagulation after a shared decision-making process. However, there remain significant challenges in left atrial appendage occlusion therapy related to patient selection, the procedure itself, and postprocedural patient management decisions. In this review article, we discuss some of these challenges in a case discussion–based approach.

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Atrial fibrillation (AF) accounts for most embolic strokes, especially in elderly individuals. It has major societal implications for our aging population, affecting approximately 7 million individuals in the United States.[1] Although systemic anticoagulation is known to reduce the risk of embolic stroke, a significant proportion of patients have relative or absolute contraindications to anticoagulation. Many patients who are "ideal candidates for blood thinners" do not receive anticoagulation or end up discontinuing it over the course of therapy.[2-4] In a large study involving patients with new-onset AF (n=45,092) from HealthCore Integrated Research Database from 2010 through 2013, 72.7% of the patients discontinued their oral anticoagulation, with nearly one-fourth discontinuing treatment within 3 months.[5] Likewise, only 47.5% of the novel oral anticoagulant (NOAC)–treated patients with AF in a large US commercial insurance database (n=64,661) were noted to have high adherence at 1 year.[6]

The left atrial appendage (LAA) has been implicated as the major source of emboli in more than 90% of ischemic strokes. Local site–specific therapy using the Watchman LAA closure device (Boston Scientific) was thus developed, tested in randomized controlled trials, and finally approved for the prevention of stroke in the setting of nonvalvular AF. Based on the results of pivotal trials, Food and Drug Administration (FDA) approval was granted in March 2015 for patients with nonvalvular AF at increased risk for stroke who had an appropriate reason to seek an alternative to long-term anticoagulation.[7] The Centers for Medicare & Medicaid Services, for reimbursement purposes, subsequently approved the Watchman device as an alternative for stroke prevention in patients with an elevated stroke risk ($CHADS_2$ score $\geq$2 or CHA_2DS_2-VASc score $\geq$3) who could be treated with short-term warfarin but in whom there is a rationale for avoiding long-term oral anticoagulation based on a shared decision-making process.[8] Such indications although helpful, do not take into account the nuances of clinical care for specific patients. The following clinical scenarios have been selected to illustrate some of the practical issues faced in the care of these patients and to address potential approaches to possible

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resolution. All the described cases fall under 1 of the following 4 categories: (1) preimplant patient selection criteria, (2) specific devices considered, (3) procedural performance, and (4) postimplant issues. All the patients were evaluated and the LAAO procedures were performed from January 1, 2016, through April 30, 2017, after informed consent was obtained and after a shared decision-making process had been completed.

CURRENTLY AVAILABLE STRATEGIES FOR LAAO

As the only LAAO device with randomized trial data supporting its use, the Watchman is the only FDA-approved option for LAAO. In the pivotal Left Atrial Appendage System for Embolic Protection in Patients With Atrial Fibrillation (PROTECT AF) trial, patients with nonvalvular AF (n=707) and an additional risk factor for stroke (mean $CHADS_2$ score of 2.2) were randomized 2:1 to receive dose-adjusted warfarin or LAAO with the Watchman device.[9] There was no significant difference in the primary end point of stroke, systemic embolism, and cardiovascular or unexplained death between the 2 arms (3 vs 4.9 per 100 patient-years in the Watchman group vs the warfarin group [relative risk, 0.62; 95% CI, 0.35-1.25]). However, the rate of primary safety events was higher in the Watchman arm (relative risk, 1.69; 95% CI, 1.01-3.19), including pericardial effusion (5% of the Watchman patients), major bleeding (3.8%), and device embolization (0.6%).[9] A follow-up trial, Prospective Randomized Evaluation of the Watchman LAA Closure Device in Patients With Atrial Fibrillation Versus Long-term Warfarin Therapy (PREVAIL), was then performed due to safety concerns raised by the FDA after the results of the PROTECT-AF trial.[10] A total of 407 patients (with a relatively higher $CHADS_2$ score of 2.6 compared with PROTECT-AF) were randomized in a 2:1 manner to receive the Watchman device and warfarin. The Watchman device was demonstrated to be noninferior to warfarin in terms of the co-primary efficacy end point of stroke or systemic embolism more than 7 days after randomization.[10] Procedural complications decreased to 4.2% compared with 8.7% in the PROTECT AF trial (P=.004).[10]

ARTICLE HIGHLIGHTS

- There remain significant challenges in left atrial appendage occlusion therapy related to patient selection, the procedure itself and post-procedural patient management decisions. In this review article, we discuss some of these challenges in a case-discussion based approach.
- The article provides an overview of both approved and investigational left atrial appendage occlusion therapies and their role in various patient populations and/or left atrial appendage anatomies.
- We provide some of the limitations of randomized data on approved left atrial appendage occlusion therapies and its impact on patient selection.

Another option for endocardial LAAO is an Amplatzer cardiac plug (ACP) Amulet device (Abbott) made of nitinol mesh. The device has a distal anchoring lobe that is positioned in the LAA body and is connected by a waist to a proximal disc that seals the LAA orifice. The largest registry data for the ACP included 1047 patients and reported a 2.3% annual stroke rate in patients with the ACP device, a 59% reduction compared with the predicted rate based on the cohort's mean CHA_2DS_2-VASc score.[11] An investigational device exemption trial is evaluating the safety and efficacy of the ACP Amulet device with the objective of demonstrating its noninferiority to the Watchman device.[12]

LARIAT (SentreHEART) is a percutaneously delivered ligature that is placed around the LAA neck using transseptal endocardial and pericardial access. No postprocedural anticoagulation is required after Lariat. Lariat and other epicardial approaches for LAAO, such as the newer AEGIS (Aegis Medical), are, thus, valuable in patients with absolute contraindications to anticoagulation or unsuitable LAA anatomy for endocardial occlusion. Lakkireddy et al[13] presented the largest available data on Lariat from a multicenter registry of 712 patients, reporting procedural success in 95.5%, with low procedural mortality (0.14%). However, there have been some procedural safety concerns regarding LAA perforation and cardiac tamponade, and it is not FDA approved for this indication currently. Such patients with contraindications