Left Atrial Appendage Closure for Stroke Prevention
Emerging Technologies

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KEYWORDS

• Atrial fibrillation • Left atrial appendage closure • Stroke • Cardioembolic risk

KEY POINTS

- Left atrial appendage closure is a recognized strategy for reducing risk of stroke in atrial fibrillation without utilizing anticoagulation.
- In addition to surgical closure, a number of novel percutaneous approaches have been developed in recent years, each with distinct advantages and limitations.
- The availability of multiple approaches will allow the physician to select the optimal approach for a given patient based on physiologic, anatomic, and clinical considerations.

INTRODUCTION

Atrial fibrillation (AF) affects approximately 2.2 million people in America.[1] The most feared complication of AF is stroke. One in every 6 strokes occurs in patients with AF, with the frequency increasing with age such that 1 of every 3 patients aged 80 to 89 years with stroke has AF.[1] Most strokes in persons with AF are associated with left atrial thrombi, found in 15% to 20% of patients with nonvalvular AF, of which 80% to 90% are located in the left atrial appendage (LAA).[2,3]

To date, antiarrhythmic therapy has not been associated with a reduction in stroke risk, and until recently options were limited to vitamin K antagonism with warfarin. Warfarin reduces the risk of stroke by 60% to 70% compared with no antithrombotic therapy and 30% to 40% compared with aspirin.[1] However, the major limitation of warfarin is its narrow therapeutic window, with both supratherapeutic (15%–30%) and subtherapeutic (up to 45%) international normalized ratios being common, which are associated with increased bleeding and thromboembolic complications, respectively.[4,5] Other limitations of chronic warfarin therapy include multiple interactions with diet and medications, and management challenges surrounding invasive procedures and the use of adjunctive antiplatelet therapies. The oral direct thrombin inhibitors dabigatran and ximelagatran, and the direct factor Xa inhibitor rivaroxaban, have been demonstrated to be equivalent therapeutically to warfarin and offer a more predictable response,[6–8] while apixiban has been demonstrated to reduce mortality, stroke risk, and bleeding in comparison with warfarin.[9] However, long-term outcome data are lacking and the cost of these agents can be prohibitive. Moreover, these drugs do not eliminate bleeding risk and, like warfarin, subject an increasingly aged patient group to systemic anticoagulation, with significant bleeding complications leading to contraindications for anticoagulation in approximately 40% of subjects at risk.[10,11]

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These limitations in antithrombotic therapies have led to the development of various ways of obliterating the LAA as a strategy to reduce both stroke risk and the need for anticoagulation. This review summarizes published studies on surgical and transcutaneous approaches to LAA closure, with a focus on emerging technologies. In doing so, the impact of our current understanding of mechanisms of stroke in AF, structure and function of the LAA, and intrinsic variation in procedural techniques on the relative success and limitations of each approach are discussed.

RISK OF STROKE IN AF

Because of its anatomic complexity and sluggish blood flow during atrial arrhythmias, the LAA is presumed to be the source of thromboembolism in most cases of AF. In nonvalvular AF, thrombi are localized within the LAA on 80% to 90% of occasions.[3] By comparison, localization outside the LAA occurs in 56% of cases with valvular AF.[3] In nonvalvular AF, the best validated methods of identifying patients at risk of stroke are based largely on clinical risk factors such as the CHADS2 score, which attributes risk based on the presence of Congestive heart failure, history of Hypertension, Age greater than 75 years, Diabetes mellitus, and prior Stroke or transient ischemic attack.[12,13] Each factor adds 1 point to the risk score, except for stroke or transient ischemic attack (TIA), which adds 2 points. The CHA2DS2-VASc score[14] also incorporates vascular disease (defined as prior myocardial infarction, peripheral artery disease, or aortic plaque), age 65 to 74 years, and female gender as additional risk factors to the CHADS2 score, and may have improved performance in identifying further subsets at increased risk for thromboembolism.[15] Increasing CHADS2 score has been shown to be associated with increasing likelihood of having LAA thrombus or sludge (ie, dense spontaneous echo contrast present throughout the cardiac cycle) on transesophageal echocardiography (TEE),[16] which is thought to reflect a prethrombotic state from sluggish LAA flow and is a known risk factor for stroke.[17–19] Structural changes in the LAA, with endothelial damage, inflammation and fibrosis, left atrial dilatation, blood stasis, and abnormal prothrombotic changes in platelet function and the coagulation system, have all been described in AF and have been suggested to provide the link between AF burden,[19,20] clinical risk factors for stroke, and the presence of atrial thrombus in this population.[21,22]

Of importance, the risk factors for stroke in AF are also risk factors for atherosclerosis. Patients with AF may have LAA-dependent (LAA thromboembolism)[2,23] and LAA-independent (aortic arch, carotid, and intracerebral artery disease) stroke mechanisms (Fig. 1).[24] Given that warfarin does not significantly affect atheroembolic or arterial

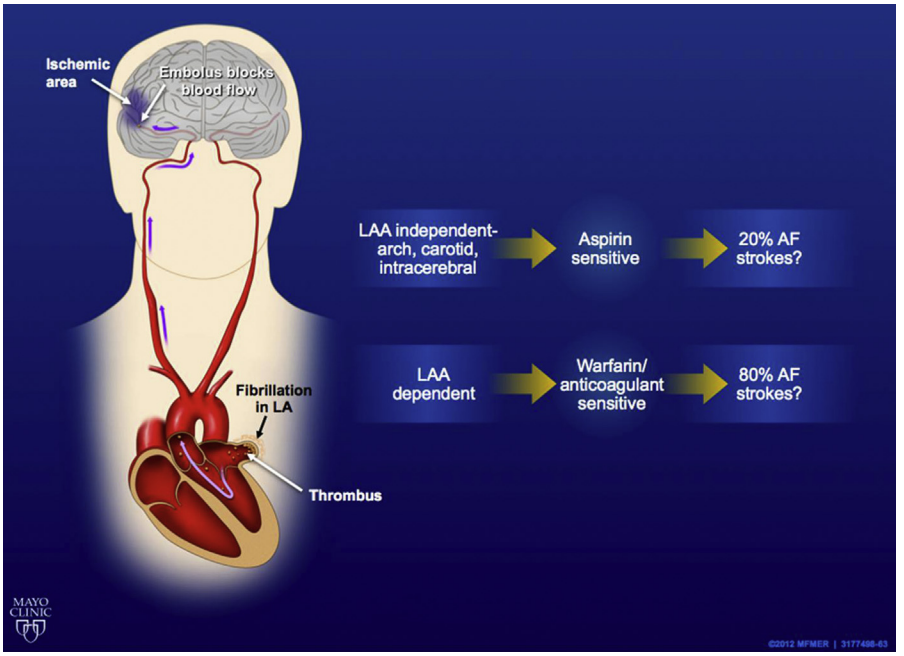

Fig. 1. Left atrial appendage (LAA)-dependent and LAA-independent stroke in atrial fibrillation (AF). (*Reprinted from* the Mayo Foundation; with permission.)