left atrial appendage closure (LAAC) has proven its safety as an effective alternative to warfarin for stroke prevention in patients with nonvalvular atrial fibrillation (NVAF).

To prevent stroke and systemic emboli in patients with NVAF, warfarin is effective but limited by its narrow therapeutic range, the need for lifelong anticoagulation monitoring, and multiple drug and food interactions, which was the impetus for the development of NOACs (nonwarfarin oral anticoagulants). LAAC is now performed across the world. The procedure prevents thromboembolism, particularly ischemic cardioembolic stroke, by occluding the LAA orifice with a specific device, because transesophageal echocardiography and autopsy studies suggested the LAA is the major source of thromboembolism in patients with NVAF, which led to the

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Figure 1. (Upper) Kaplan-Meier curves for the primary efficacy and safety endpoints. The primary efficacy outcome was stroke, systemic embolization, or cardiovascular death. The primary safety outcome was a composite of major bleeding events and procedure-related complications. (Lower) Kaplan-Meier curves for (A) ischemic stroke, (B) cardiovascular mortality, and (C) all-cause mortality. CI, confidence interval; HR, hazard ratio; RR, rate ratio. (Reproduced with permission from Reddy VY, et al.)

Percutaneous Left Atrial Appendage Closure for Non-Valvular Atrial Fibrillation
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The concept of using the Watchman device (Boston Scientific, MA, USA) is proven in the USA and other European countries. The self-expanding device composed of a nickel-titanium frame and permeable polyester fabric cap is designed for percutaneous delivery via a transseptal sheath to the LAA. After device deployment, the patient takes aspirin and warfarin for 45 days to facilitate endothelial coverage, followed by dual antiplatelet therapy using aspirin and clopidogrel, and after 6 months, single antiplatelet therapy, aspirin, is used.

The most representative trial to demonstrate this evidence was PROTECT AF. “Local” therapy by device-based LAAC was compared with systemic therapy with warfarin in this randomized clinical trial in patients with NVAF and at least 1 CHADS2 score. The trial revealed noninferiority of LAAC to warfarin for prevention of stroke, systemic embolism, and cardiovascular or unexplained death at 2 years follow-up. These findings also proved the hypothesis that in NVAF, ischemic stroke occurs mostly as a result of embolism of thrombus from the LAA, although the role of the LAA had been seldom elucidated. In addition, after 3.8 years of follow-up in patients with NVAF at elevated risk for stroke, percutaneous LAAC met the criteria for both noninferiority and superiority, compared with warfarin therapy (Figure 1), for preventing a combined outcome of stroke, systemic embolism, and cardiovascular death, as well as superiority for cardiovascular mortality and all-cause mortality. In detail, LAAC reduced the relative risk of the composite endpoint of stroke, systemic embolism, and cardiovascular death by 40% (1.5% absolute reduction) compared with warfarin anticoagulation. Besides, this device-based strategy was associated with a 60% relative risk (1.4% absolute reduction) reduction of cardiovascular death and 34% relative risk reduction (5.7% absolute reduction) in all-cause death.

The primary composite safety endpoint included procedure-related events in the device group (pericardial effusion requiring intervention or prolonged hospitalization, procedure-related stroke, or device embolization) and major bleeding in both groups (intracranial or any bleeding requiring transfusion). The rate of composite primary safety events was similar in the 2 groups, although Kaplan-Meier analysis revealed differences in the temporal distribution of these events between the groups (Figure 1). The most frequent adverse events were serious pericardial effusions and major bleeding, so we need to be cautious in proceeding with this preventive strategy for stroke. Also, procedure-related complications are decreasing in frequency with operator experience.

Regarding NOACs, they are noninferior to warfarin for ischemic stroke reduction and superior for hemorrhagic stroke and all-cause mortality, but they have an increased risk for gastrointestinal bleeding. As with warfarin, the effectiveness of these drugs depends on patient adherence. For patients who are poor candidates for long-term oral anticoagulation, percutaneous LAAC is a device-based alternative for stroke prophylaxis that is not dependent on patient adherence. One of the most important things about this strategy is that most patients can stop lifelong anticoagulation following Watchman device implantation.

Thus, LAAC with the Watchman device as well as NOACs has the potential to change the treatment paradigm for patients with nonvalvular AF who are at risk of stroke. In a recent analysis, both novel therapies demonstrated cost-effectiveness relative to warfarin (Figure 2), but only LAAC demonstrated development of mechanical approaches to closing the LAA.

PROTECT AF randomized LAAC against warfarin; however, the advent of NOACs has raised questions about their comparative safety and efficacy vs. LAAC. It would not be appropriate to compare these results with those for the new oral anticoagulants, and the relevancy of these results is highlighted by warfarin’s current role as the most commonly used agent for stroke prophylaxis in NVAF. It would be similarly inappropriate to generalize the results of this trial to other LAAC devices; they should be compared directly with either the device or anticoagulation before concluding relative efficacy and safety because of differences in device design.

Figure 2. Warfarin vs. NOACs vs. LAAC: cumulative cost and time to cost-effectiveness following treatment initiation. Average total cumulative cost per patient over 20 years. Left atrial appendage closure (LAAC) becomes less costly than nonwarfarin oral anticoagulants (NOACs) at 5 years and less costly than warfarin at 10 years. (Reproduced with permission from Reddy VY, et al.)
cost savings by year 10 relative to warfarin and by year 5 relative to NOACs.10

In this issue of the Journal, Kim et al11 report their Korean registry data of LAAC using the Watchman device as well as the Amplatzer Cardiac Plug (St. Jude Medical Inc, MN, USA) implantation. What we learn is the real-world acute success rate of this procedure in Asian patients, and the prevalence of periprocedural safety events, which we have to make as few as possible. The reported data from the Korean registry should be referred to whenever we start the program, because this is the first evidence from an Asian country regarding this technology. If we could thoroughly achieve a diminution of adverse events during or after LAAC, this therapy could fulfill the unmet needs of patients with NVAF who have both bleeding and stroke risks under anticoagulant usage, and could cause a Copernican Revolution in the management of AF.

References