EDITORIAL

Left Atrial Appendage Closure — Another Overused Method in Cardiology?

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Untreated atrial fibrillation carries an approximately 3 to 5% annual risk of ischemic stroke. Long-term oral anticoagulation therapy decreases this risk to 1.7% with warfarin and to 1.5% with edoxaban, as shown in the ENGAGE AF-TIMI 48 (Effective Anticoagulation with Factor Xa Next Generation in Atrial Fibrillation–Thrombolysis in Myocardial Infarction 48) trial, the largest such trial to date (1105 patients).[1] The price to be paid is an annualized rate of major bleeding of 2.75 to 3.43%, a well-known complication of long-term oral anticoagulation therapy. Because most ischemic strokes in atrial fibrillation originate from left atrial appendage thrombi, closure of this diverticulum may decrease the stroke risk without increasing the bleeding risk. However, the decision to implant a left atrial appendage occluder device is similar to the choice presented to the mythical Odysseus: to avoid Scylla (bleeding) he had to face Charybdis (periprocedural complications).

The PRAGUE-17 (Left Atrial Appendage Closure versus Novel Anticoagulation Agents in Atrial Fibrillation) trial showed the noninferiority of percutaneous left atrial appendage closure to oral anticoagulation during 4 years of follow-up among 402 patients with a mean age of 73 years.[2] Now, Landmesser and colleagues present in the *Journal* the results of the landmark CLOSURE-AF (Catheter-Based Left Atrial Appendage Closure in Patients with Atrial Fibrillation at High Risk of Stroke and Bleeding as Compared with Best Medical Therapy) trial,[3] which enrolled 888 patients with a median age of 79 years. Their conclusion differs from that in the PRAGUE-17 trial: left atrial appendage closure was not noninferior to physician-directed best medical care over a 3-year follow-up period.

How can the difference in findings between the CLOSURE-AF trial, which provides a strong word of caution for the widespread use of percutaneous left atrial appendage closure, and the PRAGUE-17 trial be explained? Patients who were enrolled in the CLOSURE-AF trial were 6 years older and potentially more frail than those enrolled in the PRAGUE-17 trial and had 1 less year of follow-up. The risk of periprocedural complications was high in CLOSURE-AF (5.7%), and surprisingly, major bleeding occurred slightly more often in the closure (device) group than in the medical-therapy group. This difference was mainly attributable to 23 cases of major periprocedural bleeding among patients in the device group, including 5 cases that involved pericardial tamponade. Also, the numerical excess of deaths from cardiovascular causes in the device group as compared with the medical-therapy group (65 vs. 51) may also be a warning sign.

The findings in the CLOSURE-AF trial are very important and should have immediate clinical effect. The message for the clinician is clear: left atrial appendage closure failed to fulfill its theoretical promise to become an alternative treatment to best medical therapy — at least for older patients such as those enrolled in the trial. Best individualized medical therapy should remain standard treatment for older patients. One may speculate that left atrial appendage closure devices may still be considered in younger patients, in whom, theoretically, avoiding anticoagulation therapy during very long follow-up may lead to clinical benefit by reducing the cumulative bleeding risk.

The left atrial appendage closure device is just one recent example of an interventional device

entering the clinical cardiology realm on the basis of borderline evidence, similar to the use of renal denervation procedures to treat hypertension. Despite two negative trials, renal denervation is now reimbursed in many countries, and owing to the high prevalence of hypertension, it has the potential to become one of the most overused procedures in medicine unless rigorously controlled. The SYMPLICITY HTN-3 trial did not show a significant reduction of systolic blood pressure in patients with resistant hypertension 6 months after renal-artery denervation as compared with a sham control.[4] The PRAGUE-15 trial showed that in patients with true resistant hypertension, adding spironolactone to the medical regimen was more effective than renal denervation with regard to blood-pressure reduction over a period of 24 months.[5]

The concept of widespread use of interventions despite the absence of convincing clinical evidence also applies to other procedures, such as percutaneous coronary intervention (PCI) for chronic total occlusions. Randomized trials have shown an absence of any prognostic benefit or improvement in left ventricular function after PCI for a chronically occluded coronary artery, and the largest trial (834 patients) showed no difference in the incidence of major adverse cardiovascular events with PCI as compared with medical therapy in persons with chronic total occlusion. Despite the absence of evidence, this intervention is widely performed worldwide.[6] Thus, the CLOSURE-AF trial is extremely important because it provides a highly objective real-life assessment of outcomes among patients treated with left atrial appendage closure devices. The trial also provides an example for other rigorous, academic, industry-independent trials enrolling patients to provide evidence (either positive or negative) for some of the above-mentioned procedures.

Medicine in the 21st century is evolving more and more technically, sometimes for the benefit of patients and sometimes despite the absence of clear benefit. Financial incentives, together with a wide interest among health care staff to work on the cutting edge of current techniques, may lead to overuse of some interventional procedures. All physicians should be aware of society guidelines, and in the decision-making process for each patient, they should keep in mind the overall clinical benefit of an interventional procedure from a common-sense perspective. In general, the benefit from any percutaneous intervention in cardiology is often the greatest with regard to the most acute or life-threatening problem the patient is facing. In contrast, in clinical situations in which the patient's life is not directly at risk and the symptoms are controllable by medical treatment, conservative management should always be considered to be an equally effective alternative.

Disclosure forms provided by the author are available with the full text of this editorial at NEJM.org.

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This editorial was published on March 18, 2026, at NEJM.org.

1. Giugliano RP, Ruff CT, Braunwald E, et al. Edoxaban versus warfarin in patients with atrial fibrillation. N Engl J Med 2013;369:2093-104.
2. Osmancik P, Herman D, Neuzil P, et al. 4-Year outcomes after left atrial appendage closure versus nonwarfarin oral anticoagulation for atrial fibrillation. J Am Coll Cardiol 2022;79:1-14.
3. Landmesser U, Skurk C, Kirchhof P, et al. Left atrial appendage closure or medical therapy in atrial fibrillation. N Engl J Med. DOI: 10.1056/NEJMoa2513310.
4. Bhatt DL, Kandzari DE, O'Neill WW, et al. A controlled trial of renal denervation for resistant hypertension. N Engl J Med 2014;370:1393-401.
5. Rosa J, Widimský P, Waldauf P, et al. Renal denervation in comparison with intensified pharmacotherapy in true resistant hypertension: 2-year outcomes of randomized PRAGUE-15 study. J Hypertens 2017;35:1093-9.
6. Lee SW, Lee PH, Ahn JM, et al. Randomized trial evaluating percutaneous coronary intervention for the treatment of chronic total occlusion. Circulation 2019;139:1674-83.

DOI: 10.1056/NEJMe2518067