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Time to Remove the Left Atrial Appendage at Surgery

LAAOS III in Perspective

Subodh Verma, MD, PhD; Deepak L. Bhatt, MD, MPH; Elaine E. Tseng, MD

Cardioembolic strokes are larger and associated with higher mortality when secondary to atrial fibrillation (AF).[1] Systemic anticoagulation, with vitamin K antagonists (VKAs) or direct oral anticoagulants, effectively reduces thromboembolic events,[2] but is limited by bleeding, poor adherence, contraindications, drug interactions, and therapeutic variability (particularly with VKA). Even when used optimally, however, residual ischemic stroke risk persists.[3]

Imaging and postmortem studies suggest that >90% of thrombi in nonvalvular AF are found in the left atrial appendage (LAA) and are causally related to ischemic strokes. LAA elimination may be an alternative or adjunct to systemic anticoagulation to provide a permanent preventive solution, while recognizing that the pitfalls of LAA management could be additional fluid retention attributable to atrial natriuretic peptide disruption, incomplete closure resulting in residual flow, and possible interference with the left circumflex artery. Procedural success of LAA management is typically determined by the absence of any residual blood flow between the LAA and the left atrium and a residual LAA neck (ie, stump) <1 cm.

Percutaneous LAA occlusion has been evaluated in trial settings wherein patients were randomly assigned to LAA occlusion versus VKA (PROTECT AF [Watchman Left Atrial Appendage System for Embolic Protection in Patients With Atrial Fibrillation], PREVAIL [Evaluation of the Watchman Left Atrial Appendage (LAA) Closure Device in Patients With Atrial Fibrillation Versus Long Term Warfarin Therapy]) or direct oral anticoagulants (PRAGUE-17 [Left Atrial Appendage Closure vs. Novel Anticoagulation Agents in Atrial Fibrillation]).[3] In the former, percutaneous LAA occlusion was noninferior to VKA and the benefit appeared to be driven primarily by reducing intracerebral bleeding with LAA occlusion, with a suggestion that there may have been higher device-related thrombotic/ischemic events. In patients with AF and a history of significant bleeding or an event on oral anticoagulation, PRAGUE-17 demonstrated similar rates of strokes in patients treated with percutaneous LAA occlusion or direct oral anticoagulant therapy, although there were significant implant-related complications (≈5%). Guidelines thus provide a weak recommendation to consider percutaneous LAA occlusion in patients with nonvalvular AF who are at moderate to high risk of stroke and have absolute contraindications to oral anticoagulation.[3,4]

Surgical LAA occlusion, in particular, if performed as an adjunct to a planned cardiac surgery, is an attractive proposition in patients with concomitant AF. However, the observational data have been unclear, resulting in weak recommendations for concomitant surgical LAA occlusion in patients with AF undergoing open chest surgical procedures who are deemed ineligible for oral anticoagulation.

In the LAAOS III trial (Left Atrial Appendage Occlusion Study III), Whitlock et al[5] provide results from the much-anticipated trial of LAA occlusion performed concomitantly in patients undergoing cardiac surgery, plus planned postoperative oral anticoagulant therapy. Specifically, 4811 patients with a history of AF and CHA_2DS_2-VASc score of ≥2 who were scheduled to undergo

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Correspondence to: Subodh Verma, MD, PhD, Division of Cardiac Surgery, 8th Floor, Bond Wing, St. Michael's Hospital, 30 Bond St, Toronto, ON, M5B 1W8, Canada. Email subodh.verma@unityhealth.to

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cardiac surgery were randomly assigned to LAA occlusion (using any closure technique-surgical amputation, stapler, closure device, or double-layer linear closure from within; n=2379) versus no LAA occlusion (n=2391; Figure). Patients were expected to receive appropriate guideline-recommended stroke prevention therapies postoperatively, including anticoagulation. The mean age of the cohort was 71 years; the distribution of permanent, persistent, and paroxysmal AF was ≈30%, 20%, and 50%, respectively. The CHA_2DS_2-VASc score was 4.2±2, and about one-half of the population was treated with a VKA or direct oral anticoagulant preoperatively. One-fifth underwent isolated coronary artery bypass surgery, whereas 65% had a valve procedure performed, of whom 36% had a mitral valve intervention. The trial was stopped early for efficacy with a mean follow-up of 3.8 years. At discharge, ≈80% of the patients were prescribed an anticoagulant. The primary outcome, comprising the composite of ischemic stroke or systemic embolism, occurred in 7.0% in the no-occlusion group and 4.8% in the occlusion group, consistent with a 33% relative risk reduction (hazard ratio, 0.67 [95% CI, 0.53–0.85]; *P*=0.001). The benefit on the primary outcome was driven largely by a reduction in ischemic stroke (hazard ratio, 0.66 [95% CI, 0.52–0.84]). All-cause strokes were also reduced (hazard ratio, 0.63 [95% CI, 0.50–0.80]). Death, myocardial infarction, major bleeding, and hospitalization for heart failure were not different between groups.

What are the key implications and unanswered questions from LAAOS III? The trial provides evidence that LAA occlusion should now become standard of care in patients with a history of AF undergoing cardiac surgery. The procedure can be performed safely, without a significant increase in cardiopulmonary bypass or cross-clamp time, mediastinal bleeding, or reoperation rate. Although only patients undergoing on-pump surgery were enrolled, if technically feasible, there is no reason to suspect that a similar benefit would not be seen with off-pump surgery. The benefits were consistent across the various subgroups studied, in general, including those with a CHA_2DS_2-VASc score >4 or ≤4. The results extend to patients in sinus rhythm if they had a documented history of AF or atrial flutter. Consistent benefits were observed in patients irrespective of whether concomitant AF ablation was performed. The advantages on the primary outcome were much greater beyond 30 days, emphasizing that early postoperative strokes are likely related to surgical intervention (such as aortic cross-clamping) as opposed to cardioembolism. Although no heterogeneity was observed in patients undergoing valve surgery, specific details about the mitral valve group were not provided. This is important, because, in the setting of valvular AF (particularly mitral), the LAA is the source of thrombi in ≈40% of cases (unlike nonvalvular AF, ≈90%). Furthermore, these data only apply to concomitant cardiac surgery and do not provide guidance on stand-alone surgical (or percutaneous) LAA closure. Although the data provide evidence of an additive benefit to oral anticoagulation, the question of whether LAA occlusion can be an alternative to oral anticoagulation remains unanswered. Although VKA was the most prescribed anticoagulant at discharge, the reasons why ≈20% of patients were not prescribed anticoagulation at discharge is unclear. Why patients undergoing mechanical valve replacement were excluded remains unclear, but, in our opinion, this should not limit the generalizability of the results to this population. It is notable that there was no significant increase in the rates of hospitalization for heart failure. This is important, because the LAA is a source of atrial natriuretic peptide, and it has been postulated that LAA removal may promote salt/water retention and worsen this outcome. Last, the early termination may have inflated the observed benefits.

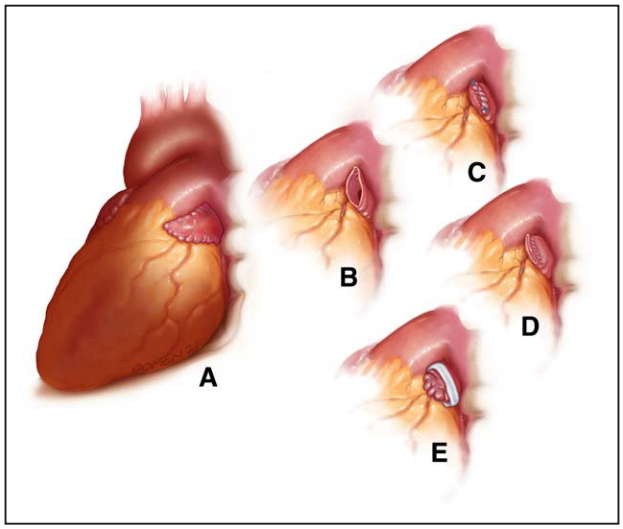

Figure. Views of the left atrial appendage before and after surgical exclusion.
A, Intact left atrial appendage. **B**, Resected left atrial appendage before closure. **C**, Left atrial appendage after sutured amputation. **D**, Left atrial appendage after stapled excision. **E**, Left atrial appendage after clip application.

LAAOS III provides evidence from the largest and non–industry-funded trial to support the additive benefits of surgical LAA occlusion on stroke prevention, when performed in patients with a history of AF or atrial flutter and CHA_2DS_2-VASc score ≥2 and is followed through with anticoagulation. This strategy yields a number needed to treat for 5 years of 37 and was consistent in patients with all types of preoperative AF, those with and without concomitant ablation and across various modes of surgical closure. These data do not directly endorse percutaneous LAA closure, nor do they speak to stand-alone surgical LAA occlusion.

ARTICLE INFORMATION

Affiliations

Division of Cardiac Surgery, St. Michael's Hospital, University of Toronto, ON, Canada (S.V.). Division of Cardiovascular Medicine, Brigham and Women's Hospital

Heart & Vascular Center, Harvard Medical School, Boston, MA (D.L.B.) Division of Cardiothoracic Surgery, University of California San Francisco and San Francisco VA Medical Center, San Francisco, CA (E.E.T.).

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