SILENT CEREBRAL EMBOLISM DURING CATHETER ABLATION OF ATRIAL FIBRILLATION
HOW CONCERNED SHOULD WE BE?

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Radiofrequency catheter ablation is recommended with increasing frequency as part of a treatment regimen for both paroxysmal and persistent forms of symptomatic atrial fibrillation (AF), largely because of the relatively poor efficacy of antiarrhythmic medications \(^1\) and trials showing improvement in quality of life and reduction in AF in selected patients. \(^2\) The ongoing Catheter Ablation Versus Antiarrhythmic Drug Therapy for Atrial Fibrillation (CABANA) trial is a randomized, multicenter study currently enrolling up to 3000 patients to test whether a treatment strategy of left atrial catheter ablation for the purpose of eliminating AF will be superior to current medical therapy for reducing total mortality in patients with AF. \(^3\) For catheter ablation to be superior, procedural complications need to be minimized.

*Article see p 1667*

Catheter ablation for AF is infrequently associated with clinically apparent thromboembolism. Cappato et al \(^4\) reported a 0.94% incidence of stroke or transient ischemic attack in a worldwide survey of AF ablation, and Scherr et al \(^5\) reported a 1.8% incidence overall with a higher incidence in patients with CHA2DS2 score ≥2 or prior transient ischemic attack. In a study at the Brigham and Women’s Hospital, we observed a 0.7% incidence of stroke or transient ischemic attack. \(^6\) It is important to recognize that the incidence of asymptomatic embolic events may be much higher. In this issue of *Circulation*, Gaita et al \(^7\) report a 0.4% incidence of clinically apparent stroke and a 14% incidence of silent cerebral embolism in 234 consecutive patients studied by cranial MRI the day after the ablation procedure. Qualified neurologists confirmed the absence of signs or symptoms of stroke. An 11% incidence of silent cerebral embolism was also reported earlier this year in a smaller cohort of 53 patients by Schrickel et al, \(^8\) who found coronary artery disease, left ventricular hypertrophy, and left ventricular cavity dilation to be predictive.

The origin of thrombus formation and embolization during catheter ablation is partially understood. First, without imaging to detect it, a preexisting thrombus may lurk in the left atrial appendage, vulnerable to blind dislodgement by catheter manipulation. In the Gaita et al study, all patients had transesophageal echocardiography to exclude this possibility. In addition, radiofrequency lesions can create a nidus for thrombus formation. Gaita et al used an irrigated-tip ablation catheter, which has been suggested to reduce the risk of thrombus formation from radiofrequency energy application. \(^9\) Furthermore, operators who use intracardiac echocardiography are well aware that a thrombus may form on sheaths and catheters, often before placement in the left atrium. This observation has led to higher-intensity periprocedural anticoagulation in many electrophysiology laboratories, in addition to constant infusion of heparinized saline through sheaths placed in the left atrium. In our laboratory, we perform left atrial ablation procedures with an international normalized ratio target of 2.5 and activated clotting time target >350 seconds and have not seen a higher incidence of cardiac tamponade or other major bleeding complications. We usually administer unfractionated heparin immediately after sheath placement in the femoral veins and before catheters are introduced or transseptal puncture is performed. Ren et al \(^10\) showed that target activated clotting time values >300 seconds reduced thrombus formation on catheters visualized by intracardiac echocardiography. Hussein et al \(^11\) reported that of 3052 patients with mean international normalized ratio of 2.5 during the procedure, 0.1% had a clinically apparent stroke. In the Gaita et al study, warfarin was discontinued 5 days before the procedure to normalize the international normalized ratio, and the activated clotting time target was 250 to 300 seconds. Gaita et al observed a 17% incidence of silent cerebral embolism with activated clotting time values <250 seconds and 9% for values >250 seconds. Importantly, unfractionated heparin was administered after transseptal puncture, giving time for thrombus formation on a transseptal sheath. This lower level of anticoagulation may increase the risk of silent thrombus formation and embolization and has not been demonstrated to lower the risk of dangerous bleeding events. \(^5,11\) Of course, higher-intensity anticoagulation has not been demonstrated to lower the risk of silent thromboembolism, for which further study is needed.

It is well known that silent thromboembolism is associated with AF. \(^12\) Although a higher prevalence of dementia in patients with AF and without a history of stroke or transient ischemic attack suggests that silent thromboembolism may have long-term ramifications, \(^13\) the significance of silent cerebral embolism detected by MRI the day after a catheter ablation procedure is uncertain. Although thrombus is the likely offender, air or tissue fragments may also embolize. Acute thrombus formation in the setting of intense anticoag-
ulation during a procedure may not produce the same long-term brain injury as well-formed, chronic thrombus. The authors do not present follow-up cerebral imaging studies or neuropsychological testing to correlate the acute MRI findings with chronic scar or cognitive dysfunction. In fact, 38 patients in the study were undergoing repeat left atrial procedures, and preprocedural cerebral MRI scans showed no evidence of chronic scar related to prior embolic events. Statistically, one would have expected several patients to have MRI findings of chronic brain injury based on an 11% to 14% incidence of silent thromboembolism.

All of the patients undergoing catheter ablation who remained in AF after ablation were cardioverted before leaving the electrophysiology laboratory. Interestingly, the authors found that patients who required cardioversion at the end of the procedure had a 2.75-times greater risk of silent cerebral embolism. The authors conclude that electric or pharmacological cardioversion may be unsafe during catheter ablation. In a relatively well-matched cohort of 65 patients with persistent AF who did not have catheter ablation, the authors report no patients with silent cerebral embolism the day after cardioversion. The failure to convert to sinus rhythm during catheter ablation, however, may be the important variable, not cardioversion itself. In addition, patients who are receiving bridging anticoagulation may be at higher risk because of a period after sheath removal during which patients are left without anticoagulation. A randomized study of electric or pharmacological cardioversion at the end of the procedure is needed to answer the question definitively.

Certainly, we need to gather more information concerning clinically unrecognized cerebral embolism complicating catheter ablation of AF and to clarify the ramifications of these events for patients. Continued development and assessment of measures to further reduce thromboembolism, such as higher-intensity anticoagulation protocols, and technological advances, such as protective filters, are warranted.

Disclosures
None.

References

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