Editorial

ERACEing the Risk of Cerebral Embolism From Atrial Fibrillation Ablation

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Atrial fibrillation (AF) is the most common arrhythmia requiring treatment. The adverse outcomes commonly attributed to AF include symptomatic palpitations, dyspnea and exertional intolerance, and increased risk of thromboembolic complications, especially stroke. Because of the morbidity of this condition, several different treatment strategies have been derived to improve patient outcome. One of the strategies that are being used increasingly is catheter ablation. Presently, this is an aggressive, extensive ablation procedure designed to isolate triggering foci from electric conduction to the body of the atria and modifying atrial substrate to disrupt or prevent conduction/propagation of reentrant wave fronts. This procedure can be of long duration and associated with extensive myocardial destruction. Most of the ablation is performed in the systemic circulation. Because of these factors, systemic embolic events, especially stroke, have always been feared complications associated with this procedure.[1] Although the prevalence of stroke complications has been low, concern has been raised in recent years about the observation of asymptomatic cerebral embolism (ACE) on diffusion-weighted MRI.[2–4]

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ACE lesions after catheter ablation of AF were first reported by Lickfett et al[5] and since have been described by several groups. The mechanisms leading to the formation of ACE lesions have not been completely elucidated but are presumed to be because of microembolism to the small terminal intracerebral arteries.[1] The components of the microembolic material causing ACE lesions after AF catheter ablation are hypothesized to be thrombus, gas microbubbles, heat-denatured albumin microbubbles, thermal coagulum, and avulsed tissue.[6] Because this procedure does not involve catheter manipulation in the aortic root or aortic valve, dislodged calcium and cholesterol plaque probably do not have a role in ACE lesion production as is observed after transarterial valve replacement or carotid stenting. Certain catheter ablation technologies seemed to result in a higher rate of ACE lesions than others. In particular, bipolar ablation through a circular multi-electrode radiofrequency ablation system has been shown to produce ACE lesions in as many as 39% of patients in observational trials.[3,7] Therefore, it is an appealing hypothesis that techniques aimed at minimizing the risk of bubble, thrombus, and coagulum formation, especially with the multi-electrode radiofrequency catheter, might reduce the risk of ACE lesions seen after AF ablation.

In this issue of *Circulation: Arrhythmia and Electrophysiology*, Verma et al[8] endeavored to determine whether the risk of ACE lesions could be mitigated by meticulous attention to specific details during the ablation procedure. First, the investigators hypothesized that thromboembolism because of inadequate anticoagulation could be the source of ACE lesions. Intracardiac thrombus as identified by intracardiac echocardiography can be reduced with more aggressive heparin anticoagulation, especially in patients who are prone to atrial thrombus formation such as those with marked atrial enlargement and spontaneous echocardiographic contrast. Maintaining an activated clotting time >300 seconds has been demonstrated to achieve this end.[9] In addition, continuous anticoagulation with warfarin before, during, and after the procedure is associated with a trend toward lower risk of clinical stroke.[10] After these observations, the investigators only performed procedures during therapeutic vitamin K antagonist therapy and maintained activated clotting time >350 seconds with intravenous heparin throughout the procedure. Second, air introduction into transseptal sheaths has long been recognized as a contributor to adverse neurological events during catheterization procedures.[11] It is routine practice among AF ablation operators to minimize catheter exchanges, maintain a pressurized flush of heparinized saline through the sheath, and when possible, withdraw the sheath into the right atrium during left atrial catheter manipulation. However, there has not been much attention paid to the initial introduction of the catheter through the hemostatic valve in the sheath. Therefore, the investigators' practice was to submerge the hub of the introducer sheath during loading of the catheter to prevent any air entry. Finally, coagulum formation is a consequence of excess radiofrequency power delivery to the ablation electrodes leading to boiling of the blood and denaturation of blood proteins, resulting in the formation of the friable material referred to as "coagulum." Ablation with the multi-electrode radiofrequency catheter has posed particular challenges because of a problem unique to the bipolar mode of energy delivery and the circular catheter design. Experimental and clinical studies have shown that when the catheter is constrained by pulmonary venous anatomy, inadvertent radiofrequency current shunting between overlapping proximal and distal electrodes can produce excess heating at that bipole and coagulum formation.[6,12]

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To diminish this risk, the investigators inactivated the distal or proximal electrodes of the circular catheter (the electrodes that could potentially overlap) during bipolar energy delivery. With the above-procedural modifications, the ACE lesion prevalence post ablation was reduced to 1.7%, more than a 20-fold reduction in prevalence compared with published reports. The authors are to be congratulated for these superb outcomes, and their meticulous attention to detail should be an example for all of us to follow.

In addition offering strategies for reduction of ACE lesion prevalence post AF catheter ablation, this study highlighted the possible contribution of AF to the development of ACE lesions over time. Asymptomatic cerebral lesions on MRI scan are very common, reported in ≈20% of healthy elderly subjects and 50% of patients with cardiovascular disease, hypertension, and diabetes mellitus.[13] Factors that have been associated with a higher prevalence of these lesions include increasing age, female sex, a history of hypertension, diabetes mellitus, cardiovascular disease, migraine headaches, cigarette smoking, and AF[13] although at least one large population-based study did not find that AF predicted silent brain infarction.[14] When patients with nonvalvular AF were compared with age- and sex-matched controls, the prevalence of small (3–5 mm) and larger (>5 mm) asymptomatic cerebral lesions was significantly higher in the AF patients than in the controls (74.6% versus 57.7% for small and 49.3% versus 28.2% for larger lesions).[15] Another study of patients selected from a cardiovascular prevention outpatient clinic described the prevalence of silent brain infarcts as 89% in patients with a history of paroxysmal AF, and 92% in patients with persistent AF, versus 46% in control patients with no AF history. A greater number of lesions per patients was seen in those with persistent versus paroxysmal AF.[16]

The authors of the present study observed that 60% of their patients had cerebral lesions detected by MRI on their baseline scans before any catheter procedure had been done. Theirs was a fairly healthy AF ablation population with a mean age of 60±10 years, an 87% prevalence of paroxysmal AF, and a $CHADS_2$ score of 0.6±0.7. The prevalence of lesions on cerebral MRI pre-AF ablation in similar patients has been reported as 32% to 42%.[4,17,18] The variance among studies may be attributed to varying definitions of silent brain infarcts, but these findings emphasize the fact that over time, AF takes its toll. ACE lesions or silent brain infarcts have been associated with worse cognitive performance on objective testing[16] and greater cognitive decline later in life.[13,19] In fact, it has been proposed that the terms "asymptomatic" and "silent" be replaced with the term "covert" because objective evidence of neurological injury can often be uncovered with objective testing in these "asymptomatic individuals."[19] Conversely, our treatment for this condition with catheter ablation is associated with new ACE lesions and acute cognitive decline.[20]

As is often the case in medical science, we are now at a crossroads. We have good evidence that ongoing paroxysmal or persistent AF is associated with brain injury and reasonable pathophysiological mechanisms hypothesized to establish a reasonable likelihood of causality. We have a variety of therapeutic interventions including antiplatelet therapies, oral anticoagulants, suppressive antiarrhythmic drugs, left atrial appendage occlusion/obliteration, and catheter ablation, all of which might allay some of the accumulating risk of brain injury in our patients with AF. At least one of those therapies (catheter ablation) has been shown to increase the risk of brain injury in the short run but offers the greatest promise to return patients to the natural history of patients who do not have this arrhythmia. The present study offers a road map to lessen that risk and thereby shift the risk–benefit analysis in favor of catheter ablation. But ultimately, there are no data to guide our way. So we move forward boldly, basing our clinical decisions on beliefs, not science. We all hope that someday we will enter a more enlightened age of AF management.

Disclosures

None.

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