Radiofrequency catheter ablation of symptomatic arrhythmias has enjoyed unprecedented growth during the past 2 decades. This has been attributed to its high success rate in the treatment of a variety of arrhythmias with a discrete ablation target and the low complication rate observed in these procedures.\textsuperscript{1,2} Initial investigators performing radiofrequency catheter ablation were fortunate that the lesions created with this energy source were small and discrete. It was difficult to cause excessive collateral injury. Early recognition of the problem of sudden electric impedance rise and coagulum formation\textsuperscript{3} led to a number of strategies and technologies to minimize this occurrence. In contrast to supraventricular tachycardia ablation, catheter ablation of atrial fibrillation has pushed the limits of our ablation technologies and has shifted the ratio of efficacy to risk in an unfavorable direction.\textsuperscript{4} Aggressive limits of our ablation technologies and has shifted the ratio of efficacy to risk in an unfavorable direction.\textsuperscript{4} Aggressive ablation with extensive linear ablation, ablation of complex fractionated atrial electrograms, and empirical isolation (debulking) of the posterior left atrial wall\textsuperscript{5} have improved procedural success in patients with persistent atrial fibrillation. But with a greater volume of myocardial injury and a greater surface area of disrupted left atrial endocardium from the ablation, it is not surprising that procedure-related complications, especially embolic complications, are more prevalent.

The initial observations of the appearance of new asymptomatic cerebral embolism (ACE) lesions on diffusion-weighted MR imaging scans after radiofrequency catheter ablation of atrial fibrillation were striking\textsuperscript{6,7} but should not have been unanticipated. The ACE lesions observed are attributed to cerebral microembolism and have been widely reported after procedures, such as cardiopulmonary bypass,\textsuperscript{8} carotid artery stenting,\textsuperscript{9} and trans aortic valve replacement.\textsuperscript{10} The fact that ACE lesions have not been reported previously with radiofrequency ablation either has been because of good fortune or simply because of our failure to look. In any case, the issue is now upon us, and it is incumbent on us to define the source of ACE lesions and do the best to mitigate this risk going forward.

In this issue of Circulation Arrhythmia and Electrophysiology, Nagy-Baló et al\textsuperscript{11} describe the occurrence of microembolic signals (MES) on transcranial Doppler during pulmonary vein isolation for the treatment of atrial fibrillation catheter ablation using 2 different ablation technologies and 2 different anticoagulation regimes. They observed that the prevalence of MES was lower in patients being ablated with a cryoballoon ablation catheter compared with patients ablated with a multipolar duty cycle radiofrequency pulmonary vein ablation catheter (PVAC). The difference was specifically attributable to higher MES production during the period of radiofrequency energy delivery with the PVAC compared with the period of cryotherapy with the cryoballoon. It is difficult to know whether the higher rate of MES with PVAC might or might not be offset by a higher chronic procedure success rate with this technology because the long-term outcome of these procedures was not reported. Higher success rates might warrant acceptance of a small hypothetical increased risk. Patients treated with a more aggressive anticoagulation regimen (anticoagulation time, $>$320 seconds) had fewer MES than those receiving the conventional anticoagulation regimen (anticoagulation time, $>$250 seconds). Also, ablations with simultaneous activation of electrodes pairs 1 and 5 of the PVAC catheter had a higher MES count than ablations where one of these electrode pairs was inactivated.

The observations in this small study have value and are consistent with other reports.\textsuperscript{12-14} Previous studies using older ablation generator software and delivery of radiofrequency energy in bipolar fashion to all 5 electrode pairs on the PVAC have reported an excess prevalence of ACE lesions on diffusion-weighted MR imaging scans compared other ablation technologies, such as irrigated radiofrequency ablation or cryoballoon catheter ablation.\textsuperscript{15,16} New temperature feedback power control algorithms now help to minimize power overshoot, and the important interaction of electrodes 1 and 10 (from electrode pairs 1 and 5) has been better characterized. It has been observed that when the PVAC catheter loop is constrained by the pulmonary vein anatomy and RF is delivered in the bipolar mode with electrodes 1 and 10 in close proximity, excess current can be delivered to the 1 to 10 bipole and char may embolize from these electrodes.\textsuperscript{14} Inactivation (or removal) of electrode 10 in newer system iterations should lessen this complication in the future. Whether pulmonary vein ablation with the new PVAC system will have a greater, equivalent, or lesser propensity for microembolism than ablation with the cryoballoon, and how the 2 systems will fare with long-term procedure efficacy remains to be seen. But the...
important lesson demonstrated by this study is that monitoring MES count with transcranial Doppler as a surrogate marker for ACE risk may be a useful metric for gauging microembolic risk of new ablation technologies going forward.

The exact mechanisms of ACE lesion formation after atrial fibrillation ablation are unknown, and we do not know the precise composition of the microemboli-generating MES. The possibilities include thrombus, coagulum/char, air, or steam. Tissue injury from microembolism is a function of both embolic load and longevity of the embolic material in the circulation. Regarding gaseous emboli, microbubbles generated from air entry through a transseptal sheath might be more or less dangerous than microbubbles formed from boiling blood during radiofrequency catheter ablation. Bubbles from a sheath might be larger and might have greater longevity in the circulation because of their size. Note that the rate of reabsorption of air bubbles in the bloodstream is a function of the bubble surface area (proportional to the square of the bubble radius) and the volume of gas to be reabsorbed (proportional to the radius cubed). Larger bubbles, therefore, take significantly longer to be reabsorbed than smaller bubbles. However, steam formed during overheating with excess radiofrequency energy delivery might become encased in a microbubble comprised of denatured blood proteins, and might have a significantly greater longevity on that basis. The MES observations in the study of Nagy-Baló indicate that 80% of the microemboli are gaseous, but despite the fact that gaseous microbubbles may be more prevalent, particulate microemboli would be anticipated to be more durable. Of interest, more aggressive anticoagulation reduced but did not eliminate the occurrence of MES in the present report. This supports the notion that thrombus only accounts for a minority of the particulate embolic burden seen in this setting. Techniques to reduce excess heating and char formation have succeeded in reducing the ACE prevalence, suggesting that coagulum/char embolism remains the most concerning perpetrator.

The clinical implications of ACE lesions are significant. Even though these lesions are asymptomatic, they are associated with real evidence of pathological injury. A recent study in an experimental model of the effects of gaseous and particulate microembolism demonstrated typical lesions on diffusion-weighted MR imaging and fluid attenuated inversion recovery MR images. Despite the resolution of many of these lesions by day 4 post embolism, clear evidence of ischemic injury was present on histopathologic examination of brain specimens. Severe endothelial proliferation, moderate glia cell activation, and a mild perivascular lymphocytic infiltrate were observed. Clinical studies after serial MR images post ablation demonstrate lesion resolution when the lesions are small, but more persistence when lesions are larger. It is possible that limitations of spatial resolution of MR imaging (most studies use 4–5-mm slice thickness) account for the disappearance of the acute lesions on follow-up. In the absence of focal neurological deficits, the lesions observed on MRI scans are defined as asymptomatic. However, the long-term implications of an accumulated burden of neurological injury from intracardiac interventions are unknown. There is an increasing body of evidence associating atrial fibrillation with late dementia and cognitive decline. It is hypothesized that recurrent asymptomatic thromboemboli from chronic atrial fibrillation may be the cause. As the burden of cerebral injury increases over time, from whatever source, the recovery from cerebral insult is reduced, and the likelihood of neurological degeneration increases. Thus, the double hit hypothesis states that ACE lesions earlier in life (either from chronic atrial fibrillation or catheter ablation to treat atrial fibrillation) may result in earlier cognitive decline, or worse outcomes after clinical stroke.

The stakes are high but the course is not clear. Whether medical management with optimal oral anticoagulation is the best long-term strategy, or whether aggressive efforts to eliminate atrial fibrillation with ablation procedures is preferred is a compelling question that will be seeking resolution in the years ahead. Every choice has a price. What is clear is that efforts to maximize the success rates of atrial fibrillation ablation while minimizing the extent of tissue ablation and, in turn, the risk of acute and long-term complications need to be redoubled.

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References


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Asymptomatic Cerebral Embolism and Atrial Fibrillation Ablation: What Price Victory?
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