Catheter ablation has been established as an important option in the treatment of patients with atrial fibrillation. This therapy currently carries a class I indication in patients with atrial fibrillation who have failed to respond to antiarrhythmic drug therapy and a class IIb indication in patients with paroxysmal atrial fibrillation untreated with antiarrhythmic agents (1). Although the evidence supports its role as an overall safe and effective treatment for this common arrhythmia, serious complications are not rare, and recurrent arrhythmia necessitating repeat procedures is a frequent and vexing problem (2). Tools to identify those more or less likely to gain a lasting benefit from this invasive procedure would be a welcome addition to the field.

In this issue of JACC, Neilan et al. (3) report the association of cardiac extracellular volume (ECV) with the risk of recurrent atrial fibrillation after catheter ablation. ECV is a quantitative correlate of diffuse fibrosis in the left ventricular myocardium derived from contrast-enhanced cardiac magnetic resonance. This marker has been histologically validated in a variety of conditions and can be relatively easily measured during the course of cardiac magnetic resonance (4).

This study prospectively enrolled 145 patients referred for cardiac magnetic resonance of the pulmonary vein anatomy before planned catheter ablation at a single center over 2.5 years. Patients were further selected for an existing diagnosis of hypertension. Those with diagnoses associated with a greater incidence of replacement fibrosis manifesting as overt late gadolinium enhancement, such as diabetes and cardiomyopathy, were excluded. Clinical risk factors and echocardiographic measures of cardiac structure and systolic and diastolic function were also obtained. The data were analyzed to identify correlations between ECV and other clinical predictors before ablation and for prediction of adverse events after ablation in univariate and multivariate models. The primary outcome considered was clinically-apparent recurrent atrial fibrillation at a median of 18 months.

As expected, recurrent atrial fibrillation after catheter ablation was common in this population, with the primary endpoint occurring in nearly one-third of all patients. In the analysis of baseline clinical and echocardiographic measures, ECV was significantly correlated with left atrial size, left ventricular mass, and abnormal diastolic function. Measured ECV was similar in a subset of patients imaged at basal, midventricular, and apical slices, consistent with the hypothesis that increased fibrosis in these patients is a diffuse, global process. Evidence of focal injury was quite rare, with only 2% demonstrating late gadolinium enhancement.

The primary finding of this study was the ability of an increased ECV to predict recurrent atrial fibrillation (hazard ratio: 1.29; p < 0.0001). There was evidence of a dose-effect relationship between increased ECV and risk of recurrent atrial fibrillation after ablation, with a 29% increase in the primary endpoint for every 10% increase in ECV. This finding was entirely independent of other clinical or imaging risk factors.

The authors also note a significant association between ECV and overall cardiovascular events, including heart failure and death. This combined endpoint, however, was almost wholly driven by recurrent arrhythmia, which accounted for 87% of events during follow-up. The overall incidence of heart failure and death was too low to permit truly meaningful conclusions regarding ECV and such outcomes, and this result should be interpreted with caution.
How could this information be useful in the decision-making process when contemplating ablation in a particular patient? Although the increased risk of adverse events was highly significant, the overall magnitude of that risk is modest and certainly would not warrant withholding this therapy simply on the basis of an increased ECV. This information could be of use in discussion of risks and benefits while counseling the patient about therapeutic options or potentially deciding to perform more extensive ablation of the atrium over simpler pulmonary vein isolation.

What mechanism might plausibly connect the finding of increased diffuse myocardial fibrosis in relatively remote ventricular myocardium with an increased likelihood of atrial arrhythmia? The authors speculate that fibrosis results in abnormal diastolic function by contributing to increased left ventricular stiffness, hence resulting in elevated left atrial pressure and, therefore, a greater propensity for future atrial fibrillation. This reasonable hypothesis is circumstantially bolstered by the concomitant finding of associations between ECV, atrial size, and abnormal diastolic function by echocardiography. A recent report found that invasively measured mean left atrial pressure, at least in patients without marked left atrial enlargement, predicted recurrence of atrial fibrillation. These hypothetical links would also help provide an answer to an almost unavoidable question about the choice of imaging targets in this study. Why would one look at the ventricle to get answers about an atrial problem? Visualization of replacement fibrosis as overt late gadolinium enhancement in the atria is possible, but the atrial myocardium is too thin to permit quantification of diffuse fibrosis as performed with current methods. This calls to mind the timeworn joke about a man found looking for his lost keys under a street lamp. When asked where he lost the keys, he points some distance away and replies, “Over there, but the light is better here.” The logic of this approach makes the best sense in the setting of diffuse processes—pressure, fibrosis, or other factors—affecting both atria and ventricles.

Any new advanced imaging technique must ultimately address the question: “who do I scan?” By identifying ECV as a unique and independent risk factor for successful atrial fibrillation ablation, Neilan et al. present a first step toward incorporating this measure into the evaluation of candidates for this procedure.

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