Electrophysiological abnormalities in subjects with lone atrial fibrillation – Too little, too late?

1. Electrophysiological parameters as surrogates for atrial remodeling

Arroja and colleagues present an interesting observational study providing insights into the electrophysiological characteristics of subjects with atrial fibrillation (AF) and no evidence of overt structural heart disease in this issue of the journal [1]. The authors utilized signal-averaged P-wave duration and intracardiac electrophysiological parameters (intra and inter-atrial conduction times and refractory periods) to qualify the presence of subclinical atrial structural damage (atrial remodeling) in subjects with AF. They compared the prevalence of electrophysiological parameters of atrial remodeling in subjects with AF undergoing catheter ablation to that in a control cohort of subjects without AF. The study also compared parameters of subclinical atrial remodeling in subjects with and without recurrence of AF after catheter ablation. The rationale, presumably was to test the hypothesis that subclinical atrial remodeling in subjects undergoing catheter ablation for AF may be associated with a higher incidence of AF recurrence.

As expected the surrogate parameters of subclinical atrial remodeling (P-wave duration and intracardiac electrophysiological measurements) were abnormal in subjects with AF compared to subjects without AF. This finding is not novel or unique to the current study and the fact that subjects with AF and no evidence of overt structural heart disease can have subclinical atrial remodeling has been demonstrated previously by multiple investigators [2–7]. In the current study, no differences were noted in the prevalence of surrogate parameters of atrial remodeling in subjects with and without AF recurrence after catheter ablation. Even though the study is methodologically sound and well executed, it was not designed to detect a clinically meaningful difference in surrogate parameters of subclinical atrial remodeling between subjects with and without AF recurrence. The reason for this is that the study included a homogenous group of subjects with paroxysmal AF, who in general tend to have less atrial remodeling as shown in previous mechanistic studies evaluating the prevalence of electrophysiological markers of atrial remodeling (in paroxysmal and persistent AF phenotypes) [8]. The low prevalence of electrophysiological parameters and minimal severity of atrial remodeling in subjects included in the study predicated that a relatively large sample size had to be enrolled to demonstrate a clinically meaningful difference. The number of subjects included in the study was unfortunately inadequate to answer this question.

Secondly, in the current study subjects underwent pulmonary vein isolation (PVI) by the wide area circumferential ablation (WACA) technique using either the ‘point-by-point’ ablation technique or a variable, circular-multipolar catheter. A previous mechanistic study had shown that PVI performed by the WACA technique was likely to cause greater atrial remodeling, as demonstrated by surrogate electrophysiological parameters (signal-averaged P-wave duration), compared to a segmental approach. The better success rates associated with the WACA technique was attributed to a greater degree of modification of the atrial substrate (positive remodeling) compared to the segmental PVI technique [9]. The fact that all subjects in the current study underwent PVI using the WACA technique should have resulted in nearly similar extent of atrial substrate modification after catheter ablation and should not have influenced the incidence of AF recurrence. This explanation is also supported by the observation that pulmonary vein reconnection (PVR) was the exclusive mechanism responsible for AF recurrence observed in subjects undergoing repeat catheter ablation in the current study.

2. Redefining the concept of “lone” atrial fibrillation

The authors also analyzed a subgroup of subjects with so called “lone” AF, defined as subjects below 60 years of age and without systemic hypertension. Individuals with “lone” AF were observed to have the same prevalence and severity of electrophysiological parameters of subclinical atrial remodeling like that noted in subjects with systemic hypertension or older than 60 years of age. The authors imply that electrophysiological parameters of atrial remodeling may be useful in identifying subjects at risk of developing AF without obvious risk factors or evidence of overt structural heart disease. However, this inference may be not entirely accurate.

The term “lone” AF was introduced almost seven decades ago by Evans and Swann to describe a subset of subjects with AF and no apparent risk factors known to be associated with AF [10]. This archaic term was used to describe subjects with AF in whom investigations (available at the time) did not reveal structural heart disease related to known etiologies such as ischemic heart disease, valvular heart disease etc., and implied that the AF was “idiopathic”. Peer review under responsibility of Indian Heart Rhythm Society.
However, a recent white paper on this subject has provided a series of cogent arguments dissuading the use of this terminology, primarily because a plethora of sophisticated techniques available for imaging the ultrastructural details of atrial myocardium, detecting biomarkers linked to atrial inflammation and somatic genetic abnormalities in the atrial myocardium have dramatically broadened our understanding of the pathogenesis of AF [11–17]. Therefore, it is not surprising that subjects with so called “lone” AF in the current study were also found to have electrophysiological features suggestive of atrial remodeling. This highlights the fact that all subjects with AF have abnormalities of the atrial myocardium that may be either clinically evident (overt structural heart disease) or may be detected using sophisticated techniques to evaluate the ultrastructural and genetic composition of atrial myocardium. In other words, electrophysiological testing may be a rather unsophisticated and insensitive tool to identify subjects at risk for developing AF or those with a propensity to respond sub-optimally to catheter ablation. It is increasingly apparent that all subjects with AF (in the absence of reversible causes) have abnormal atrial myocardium and that at present we simply do not have the sensitive techniques required to identify all of these abnormalities.

3. Developing strategies for detecting atrial remodeling in subjects without overt structural heart disease

The reported prevalence of AF in subjects without any overt evidence of structural heart disease is between 0.2% and 68% depending on the definition of “lone” AF, the population being evaluated and diagnostic modalities used to detect abnormalities of atrial myocardium [18–21]. The extent to which novel imaging techniques, biomarkers and genetic tests, beyond the obvious assessment of cardiac structure and function using echocardiography, should be used to detect abnormalities of atrial myocardium and predict the future risk of developing AF has not been clearly specified or widely accepted [11,22–25]. Developing an optimal strategy for diagnostic evaluation of subjects at risk of or with manifest AF is one of the most difficult challenges facing the clinician.

4. Precision medicine for the management of atrial fibrillation

The ultimate objective of the clinician is to be able to tailor therapy precisely to target the unique genetic and ultrastructural abnormalities in an individual subject with AF. The hope is that identification of atrial myocardial abnormalities very early on in the course of the disease, much before the manifestation of electrophysiological parameters of atrial remodeling or overt structural abnormalities are apparent, may offer an opportunity to better prognosticate outcomes, initiate measures for prordial prevention of AF and develop precision therapies [26–28]. In conclusion, even though the current article does not describe a novel, unique or more sensitive technique to identify subjects with atrial remodeling or prognostic outcomes in subjects undergoing catheter ablation, it definitely highlights the need for ongoing research to develop tools and strategies for early detection and targeted therapy of AF.

Disclosures
None of the authors have any disclosures or conflicts of interest for this subject.

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