EDITORIAL

Exploring the potential of pulmonary vein recordings: can they help elucidate mechanisms of paroxysmal atrial fibrillation?

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This editorial refers to 'Pulmonary vein potentials in patients with and without atrial fibrillation' by E. Hertervig et al.,† on page 692

Most episodes of paroxysmal atrial fibrillation (AF) in structurally normal human hearts are triggered by ectopic beats arising from the left atrium (LA) in the vicinity of pulmonary veins (PVs).1,2 Despite development of a rich experimental and clinical literature on PVs, the anatomy and electrophysiology of these complex structures are still incompletely understood. During embryological development, the primordial common PV shows expression of an antigen associated with the developing conduction system.3 Autopsy studies have shown that the majority of human PVs (68–96%) contain sleeves of left atrial myocardium extending beyond the LA–PV junction, with highly variable architecture.4–8 Recent studies have shown that an anatomical distinction between the PVs and the LA can be difficult to discern. Indeed, the smooth-walled LA body can be seen to have vessel wall tissue (from incorporation of PVs).9 When compared with normal controls, PVs from patients with a history of AF show only minor histopathological differences, including longer extensions of muscle sleeves into the veins. Overlapping venoatrial tissue and complex fibre geometry are thought to provide the heterogeneity and slowed conduction required for initiation and maintenance of localized re-entry.10,11 Enhanced automaticity and triggered activity may also play a part in spontaneous PV ectopy.12

Pharmacological therapy for AF has been disappointing, but catheter-based non-pharmacological approaches have shown more promise. Most catheter ablation techniques for paroxysmal AF aim to eliminate the PVs as triggers by the application of energy at the LA–PV junction13 or within the ‘antral’ areas of the LA. Appropriate procedural endpoints are crucial for any catheter-based intervention, guiding the operator to maximize efficacy and minimize risk of complications. As electrical isolation of PVs from the LA serves as such an endpoint and is a key predictor for a procedural success,14 it is important to clearly and rigorously define when isolation has been achieved.

The first step in such a determination is to clearly identify PV electrograms (EGMs), as distinct from LA EGMs. Distinguishing these signals is not always straightforward, which is perhaps not surprising, considering that we are studying extensions of LA myocardium into the veins. The right superior PV usually shows local atrial EGMs that are lower in amplitude than the PV potentials, making it relatively easy to tell the signals apart. However, catheters near the ostia of left-sided veins often record nearly simultaneous depolarization of the PV and the LA in sinus rhythm, and the far-field LA appendage EGMs can be misinterpreted as PV potentials.15 Even with coronary sinus pacing, a manoeuvre meant to increase separation between the signals, 50–60% of left-sided PVs show overlapping PV and LA potentials.16 Other manoeuvres, such as premature extrastimulus testing, LA appendage pacing, unipolar recordings, and pacing from deep within the PV, may be required to see distinct PV potentials. They exploit anatomical and physiological characteristics of the LA–PV junction to increase the conduction time into the PV and thus reveal separate potentials. Despite the difficulties distinguishing the PV from the LA EGMs, these signals may be important not only in the technique of PV isolation, but also in understanding the pathogenesis of paroxysmal AF.

Present study

Hertervig et al. aim to improve our understanding of PV potentials by comparing recordings from paroxysmal AF patients with those from control patients. Pulmonary vein
potentials are used to guide most catheter ablation procedures for paroxysmal AF and they are seen in the vast majority of patients in one or more PV ostia. The autopsy studies cited earlier showed that most PVs contain myocardial extensions, both in patients with a history of AF and normal controls. As PV potentials are thought to arise from these extensions, it is logical to ask whether they are also seen in normal controls or are related to abnormal physiology associated with AF. Until the present study and a similar one published in the abstract form, little was known about the prevalence of these potentials in non-AF patients.

**Limitations of the study**

No standard definitions exist for typical and atypical PV potentials, and the authors of this study used definitions that rely in part on qualitative determinations such as 'sharp' and 'fractionated'. This might have resulted in some classification bias, particularly because the EGMs were assessed in a non-blinded fashion. However, the investigators should be commended for their careful examination of the data and their attempt to also provide quantitative information about the timing of PV potentials. Another possible source of bias is the slight difference in the position of the recording catheter across patients, although this was addressed by multiple methods of comparing comparable position in each PV. The authors used patients with concealed accessory pathways and no history of AF undergoing catheter ablation as near-normal controls. Although these patients are known to have a predisposition for AF, and thus are an imperfect control group, there is no reason to expect them to show a lower incidence of typical PV potentials than normal controls. Thus, the magnitude of the difference in typical PV potential prevalence between the two groups, 91 vs. 11%, is perhaps even more striking. Although some might propose better definitions of typical PV potentials or classify some of the sites differently, the authors have clearly demonstrated that EGMs recorded from the PV ostia in patients with paroxysmal AF differ markedly from those with concealed bypass tracts.

**Implications**

The significance of these differences shown in this study is hard to interpret, and in fact, this study raises more questions than it answers about these curious potentials. Are they related to the cause or simply an effect of paroxysmal AF? What is the anatomic basis for PV potentials? Will other areas of the atrium (e.g. posterior wall of the LA) show similar changes and thereby reflect a process involving PV's and the 'antral' PV regions? Do they arise from structural changes in the PVs or purely from differences in conduction times? How will our new knowledge of differences in the PV potentials of AF patients fit into the vast puzzle of explaining the mechanistic basis of this perplexing arrhythmia? Will PV potentials help reveal pathophysiology that eventually aids us in devising more effective treatment of AF? Clearly the most difficult and rewarding part of our quest to understand and treat AF still lies ahead.

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**References**