Left atrial ablation pendulum swinging back towards the pulmonary veins

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This editorial refers to 'Non-inducibility post-pulmonary vein isolation achieving exit block predicts freedom from atrial fibrillation' by V. Essebag et al., on page 2550

No cardiologist today is ignorant anymore of the fact that the pulmonary vein (PV) ostia and the surrounding left atrial (LA) tissue lie at the heart of atrial fibrillation (AF). The PVs may harbor rapidly firing foci that act as triggers for the initiation of paroxysms of AF. Moreover, the region certainly also plays a key role in its perpetuation towards persistent or even permanent forms by harboring fast re-entrant wavelets that maintain the arrhythmia. Since the original reports, describing selective ablation of foci within the PV, ablative strategies have moved towards the ostia and further away from the veins into the left atrium.

However, despite intense research, it remains unclear what is the best ablation strategy for AF. Over the last decade, two main ‘schools’ have developed. The first is directed at the electrical isolation of the PV from the left atrium, a goal which is generally achieved by directing RF applications to the ostium of the veins. Therefore, it is referred to as pulmonary vein isolation (PVI). Others have taken a more anatomical approach, encircling the PV with RF lesions. The endpoint of these ablations is less uniform, although attenuation of electrogram amplitude within the ablated region might be used as an endpoint. The latter approach is more diverse among different centres, but as a group, these procedures are referred to as circumferential pulmonary vein ablation (CPVA). A clear superiority for either technique has not emerged from the limited data available comparing the two approaches.

Both have in common, however, that 20–58% of the patients have recurrent AF after 6 months to 1 year, despite attaining the procedural endpoint. It is well known that patients with paroxysmal AF have a better outcome than those with persistent/permanent AF, but few other clinical and no procedural identifiers are available to predict the effect of ablation. Recurrences have been attributed to more widespread arrhythmogenic disease, which has led to more elaborate and/or more aggressive ablation approaches with the inclusion of linear lesions, ablation of zones with fractionated electrograms, and/or elimination of vagal ganglionic plexi. Although slightly more effective, the downside of these more aggressive strategies is a higher major complication rate (like fatal LA-oesophageal fistula) or development of LA tachycardia that can be more symptomatic than the original AF and is difficult to ablate.

Over the last 2 years, it has become clear that the extent of LA–PV connections is related to arrhythmogenesis, that isolation of all four PVs leads to non-inducibility of AF in a majority of patients, that most recurrences (>80%) are due to re-conduction between a previously isolated PV and the LA, and that repeat isolation results in a reasonable long-term success rate. In fact, the recognition of the importance of PV isolation has resulted in a convergence of both ablation approaches: many groups using CPVA now also assess electrical isolation of the PV, whereas groups relying on PVI apply energy as much as possible outside of the PV ostia to prevent PV stenosis. The question, therefore, is raised in which patients ablation, aimed at PV isolation, might suffice and which characteristics might predict AF recurrence despite complete isolation of all four PVs.

Essebag et al. report on behalf of the group of Dr Mark Josephson (Boston) on a series of 102 consecutive patients who were treated with an electrophysiologically guided approach resulting in complete bidirectional isolation of all PVs. On top of ensuring conduction block from LA to PV, they also verified the absence of conduction from PV to LA by elaborate pacing from all 10 to 14 bipoles on a multi-electrode circular catheter positioned in the proximal PV. Interestingly, their study shows that AF inducibility remaining after this isolation is a predictor of recurrent AF, with an odds ratio of 3.84. The study confirms other single-centre reports on the predictive value of non-inducibility of AF after PVI or CPVA with additional lines. The predictive accuracy of AF inducibility is of similar magnitude as that of the type of prior AF (paroxysmal vs. persistent/permanent). Not only AF induced at baseline but also during infusion of high doses of isoproterenol was predictive. Because ~50% of the patients were only induced during isoproterenol administration, these findings indicate that...
testing under isoproterenol should be considered as a standard part of the evaluation protocol. Conversely, a large proportion of patients with persistent or permanent AF before ablation (thought to be the result of more general atrial electrical disease), but without inducible AF after bidirectional isolation of all PVs had an AF-free follow-up. Thus, these patients do not need more extensive ablations (CPVA, addition of linear lines, fractionated electrogram ablation), avoiding the risk of complications or pro-arrhythmia. Although determination of ablation outcome is dependent on the intensity of electrocardiographic follow-up (and hence the overall 60% AF-freedom at 1 year may be an overestimation), this has no impact on the conclusions of the authors concerning AF inducibility because the same follow-up scheme was used for all patients.

Many questions remain unanswered. The study did not systematically evaluate whether more extensive ablation in those who remained inducible after PV isolation did improve arrhythmic outcome. Forty per cent of the patients who remained inducible received additional ablation lines (21 of 52), but the rationale for doing so is not well documented, unconventional (depending on the activation sequence in the CS catheter during AF), and not randomized. The completeness of the additional lines was not assessed, although this may reflect clinical practice given the complexity to achieve and evaluate LA linear lesions. Unfortunately, re-induction of AF in those who received additional ablation lines was also not evaluated. Therefore, the impact of these additional lines on the results is difficult to assess. From the observational data the authors present, the effect of the additional lines may have been modest because freedom from AF was not significantly better (57 vs. 50% freedom from AF at 1 year, \( P = 0.52 \)). Moreover, these patients developed more LA tachycardia. Other single-centre small studies have suggested that additional lines after CPVA\(^1\) or PVI\(^6\) may render AF non-inducible and modestly improve long-term outcome. It is clear that multi-centre prospective studies will need to address this important issue.

Especially relevant for clinical practice, it remains unknown which AF patients may not at all benefit from ablation, even with the additional linear lines the authors applied.

In contrast, it is likely that a sizeable proportion of patients with AF recurrences in the study of Essebag et al.\(^9\) were due to recurrence of PV conduction, but less than 25% of the patients with recurrence underwent a repeat ablation, and the proportion with re-conduction is not reported. Studies by others have indicated that 80–97% of AF recurrence after PVI are due to re-conduction.\(^7\) If this was true for the population in this study, it would mean that the predictive power of AF inducibility at the end of the procedure might be higher. Because electrophysiological evaluation generally is not part of CPVA procedures, it is unclear whether conclusions in this regard can be extrapolated towards procedures in which PV isolation is not evaluated as an endpoint for ablation.

The burst-pacing scheme to assess AF inducibility consisted of three bursts for 5 s at 200 ms (one from the RA and two from the coronary sinus) in baseline and at high dose of isoproterenol. No data are available concerning predictive accuracy of different induction schemes, nor is there consensus about the duration and type of induced arrhythmias that are relevant from a predictive viewpoint (the authors used 10 s of induced AF/atrial tachycardia).

Given the importance of PV isolation, recent reports about transient recurrence of PV–LA conduction during administration of adenosine suggest that this manoeuvre could be used as a tool for assessing completeness of conduction block. Studies relating per-procedural findings to late outcome are however still lacking. Adenosine challenge was not performed in this study.

From the presented data, it seems prudent to limit RF applications towards the (peri-)PV region, provided bidirectional PV isolation is achieved (checked with pacing from the atrium and from different biopoles of the intra-PV circular catheter and/or with adenosine challenge) and AF is non-inducible. The major remaining question is what is the best strategy in patients with inducible AF despite complete PV isolation. Given the observation that >50% of patients with inducible AF, despite full isolation of the PV during the first ablation procedure, have no AF recurrence, the question even arises whether more extensive lesions should not always be reserved for a repeat procedure unless strong clinical predictors for recurrence with PV isolation are present (like persistent/permanent AF, moderate to major valvular heart disease, and others to be defined). In contrast, even in patients with recurrence, re-evaluation of PV conduction and re-ablation if necessary may again suffice. Future research will definitely have to focus on defining better predictor models (probably combining clinical and procedural data) that justify the higher risk of a more aggressive primary approach. For now, the pendulum towards patient-tailored and less-aggressive therapy, focusing on the PV itself, seems to be swinging back.

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References


