EDITORIAL COMMENT

Pulmonary Vein Reconnection in Patients With and Without Atrial Fibrillation Recurrence After Ablation*

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Since the landmark observation by Haissaguerre et al. (1) of rapid pulmonary vein (PV) firing at the onset of paroxysmal atrial fibrillation (AF) ablation targeting PVs and/or PV surrounding atrial tissue has remained the cornerstone approach to catheter-based treatment of AF (2). Two strategies were initially proposed, namely segmental and circumferential, with the latter more widely accepted and associated with higher success rate (3).

Previous studies reported that the long-term outcome of circumferential pulmonary vein isolation (CPVI) for paroxysmal AF (single procedure) was insufficient (4). PV-left atrium (LA) reconnection has been frequently recorded in cases with clinical recurrence (5), and as a result, was considered as the prime mechanistic insight. Reisolation of PVs has been recommended as essential strategy during the repeated procedure.

However, more a conclusive causal relationship between recovery of PV conduction and AF requires examination of control patients. Several previous studies published the unexpected and intriguing findings that in patients without clinical AF recurrence, PV reconnection had been frequently recorded in cases with clinical recurrence (5), and as a result, was considered as the prime mechanistic insight. Reisolation of PVs has been recommended as essential strategy during the repeated procedure.

In this issue of JACC: Clinical Electrophysiology, Nery et al. (9) present a meta-analysis of the prevalence of PV reconnection in patients with and without AF recurrence. Eleven studies with a total of 686 patients were included, 379 had AF recurrence and 304 were AF-free. A total of 85.5% of patients with AF recurrence had at least 1 PV reconnected, whereas the ratio was 58.6% in patients without AF recurrence. PV reconnection is modestly associated with a lower risk of AF recurrence, whereas the relationship is weaker when exclusively paroxysmal patients were included.

Nery et al. (9) comprehensively collate the reported prevalence of PV connection in patients without clinical AF recurrence. Their work is helpful for exploring the mechanism of PVI in treating AF, and is also important for the development of strategies for repeat procedures in patients with AF recurrence. The efficacy of PVI in AF treatment is reconfirmed by their analysis, but the necessity of durable PV isolation is weakened.

In critically analyzing the electroanatomic findings seen on repeat procedure, it is important to consider the extent of triggers and/or substrates that were ablated during initial ablation. Previous studies indicated that CPVI is better than segmental PVI; furthermore, larger isolation areas results in better outcome (3,10,11). This may be attributed to the following factors: 1) CPVI modifies the substrates around PV ostia, which is ideal for re-entry that are densely innervated (12); 2) CPVI lesions also have the potential to transect the ligament of Marshall (LOM), atrial ganglionated plexus (GPs) (13), and the areas where complex...
fractionated atrial electrograms (CFAEs) (14) and AF rotors could frequently be recorded (15). Thus, autonomic denervation, slow conduction modification, and rotors ablation may be executed coincidentally by wide-area circumferential ablation. Additionally, strategies without complete PV isolation (16) or non-PV foci-targeted, such as GP ablation (13), rotor-guided AF ablation (15), and linear catheter ablation without CPVI (17), have also been reported to be effective in AF treatment, suggesting multiple mechanisms involved.

An important unanswered question is whether PV isolation may warrant greater emphasis on the role of non-PV foci in patients with or without PV reconnection. At the present stage of AF ablation, non-PV foci are undervalued to a certain extent, primarily because they are infrequently induced and difficult to be localized. Additionally, a common clinical dilemma is how the lesion set should be altered if multiple veins are reconnected versus a single vein at repeat procedure. Should lesions and other foci be ablated? How would STAR-AF 2 data apply to patients during a repeat procedure?

There are several limitations to the present study. First, there was significant heterogeneity between the included studies. The time to repeat electrophysiologic study differs greatly, from 2.5 to 36 months, and more than one-half of these studies were ≤ 3 months. This problem also applies to the AF-free group. Second, the sample size in most studies included was small, especially in the AF-free group, because of the difficulty in performing electrophysiologic study in AF-free patients. The GAP-AF study has a heavy “study weight” in each analysis, whereas other studies probably had little impact on the result.

Irrespective of the uncertain unifying mechanisms of AF, PV electrical isolation is an objective, standard, and generalizable endpoint, which is widely accepted. However, it remains an anatomic and empirical strategy, rather than a patient-tailored physiologic therapy. With advances in technology, such as contact force sensing (18), new generation cryoballoon catheter (19), and hybrid epicardial-endocardial ablation (20), durable PV isolation may be more easily achieved, and therefore less relevant to the discussion of recurrence mechanisms. Further mechanistic studies are deeply important to the progress of the overall field because AF ablation remains an arrhythmia treatment in search of a consistent mechanism.

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