EDITORIAL COMMENT

Ablation of Persistent AF



Have We Come Full Circle, or Are We Chasing Our Tails?*

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Nothing is impossible to a willing heart The Proverbs and Epigrams of John Heywood (A.D. 1562) (1)

he long-term maintenance of sinus rhythm in patients in persistent atrial fibrillation (AF) remains a demanding task whatever therapeutic option is taken, but it is a challenge electrophysiologists and surgeons have enthusiastically pursued for several decades. Buoyed by the clinical success of catheter ablation of accessory pathways at the turn of the millennium, it appeared only a matter of time until AF, be it paroxysmal or persistent, would become a curable arrhythmia. Yet, despite intensive investigation, that has not yet come to pass.

The critical role of the pulmonary veins (PVs) in initiating AF is well established (2), and at least for paroxysmal AF, PV ablation appears to be sufficient to treat most patients. With single procedure success rates (defined by no recurrence of documented arrhythmia) of approximately 70% at 1 year (3) and long-term outcomes (3 to 5 years) of 80% for PV isolation (PVI) with multiple procedures (4,5), this assumption appears correct for paroxysmal AF. For patients with persistent AF (sustained arrhythmia lasting >7 days), the clinical results for PVI as a sole ablation strategy have been relatively disappointing, if not at 1 year (6), then certainly at 3- and 5-year follow-up (7,8). This has led to additional strategies to modify the atrial substrate. Due to the pioneering nature of this work, most studies driving clinical practice over the last decade have been single-center retrospective studies. Although not all agree with it, the trend continues to be more and more ablation. As the techniques have become established and positions entrenched, it is only relatively recently that systematic meta-analysis (9) and multicenter prospective randomized studies have critically examined these strategies (10).

ABLATION OF COMPLEX FRACTIONATED ELECTROGRAMS

One such prospective randomized single-center study by Vogler et al. (11) is presented in this issue of the *Journal*. Using a modified stepwise ablation strategy, they randomized patients with persistent AF to either PVI alone or to additional substrate ablation. The results suggest that additional substrate ablation offers little if anything to PVI alone, with 12-month, singleprocedure success rates of 75% and 73.8%, respectively. However, before abandoning this substrate modification for patients with persistent AF, careful interpretation of these data are required.

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Temporal classification of patients with AF is fraught with difficulty. For example, the TRENDS data demonstrated that intermittent monitoring and patient factors influence clinicians to a greater extent than expected, leading to misdiagnosis of either paroxysmal or persistent AF (12,13). As such, although the intended population was patients with persistent AF, the duration of continuous AF might have been <1 week if the patient received early cardioversion. Although inappropriate diagnosis of paroxysmal or persistent AF is likely to influence all studies of patients with persistent AF, objective measures, such as left atrial (LA) diameter and area, AF cycle length, and CHA2DS2-VASc score, suggest that the population studied was perhaps more favorable compared with those in historical retrospective

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studies (14-16). For instance, in work by the Bordeaux group, mean LA diameter and AF cycle length were approximately 47 mm and 150 ms, respectively (15); in the current study, these were 44 mm and 170 ms, respectively. Across numerous studies and groups, LA diameter and AF cycle length have consistently been independent markers of freedom from AF following ablation (5,8,17-19).

Although PVI has become standardized, comparing ablation techniques is difficult, with the devil being in the details. The move toward a more antral ablation approach has undoubtedly improved success rates (20,21), although whether this is due to additional substrate ablation, ablation of ganglionic plexi (22), or inadvertent rotor ablation (23) remains controversial. Even defining the PV antrum is difficult, let alone standardizing the complex fractionated atrial electrogram (CFAE). The technique used in the study by Vogler et al. (11) is described as a stepwise ablation technique. The original description by the Bordeaux group of stepwise ablation included PVI, which was followed by (if necessary) biatrial ablation of CFAEs, and again (if necessary), linear lesions, followed by cardioversion, with completion of linear lesions if the bidirectional block had not already been achieved. Procedural termination of AF was the endpoint. The technique used by Vogler et al. (11) was more simply PVI and then randomization to either cardioversion or CFAE ablation (24). Linear lesions were only used if a patient transitioned to a macro-re-entrant tachycardia, which occurred in approximately one-third of all cases. The Bordeaux stepwise procedure is certainly an exacting procedure, and Vogler et al. are right to comment that the modified technique used in their study may accurately represent "real-world" practice.

The data appear to support the STAR-AF II (Substrate and Trigger Ablation for Reduction of Atrial Fibrillation Trial Part II) trial, in which patients were randomized in a 1:4:4 manner to either PVI alone, additive CFAE ablation, or additive linear ablation, with no benefit shown with additional ablation compared with PVI alone (10). This was similar to an earlier randomized study in which the addition of CFAE ablation to PVI had no discernible effect regarding rhythm outcome (25). Together, these data suggest that CFAE ablation added to PVI does not confer an advantage to the patient in terms of AF-free survival, but it does increase procedural duration and bystander atrial ablation. This is substantially different from suggesting that stepwise ablation, as defined by the Bordeaux group, does not confer an advantage, especially because patients who had termination of AF by PVI alone were excluded from the analysis in the study by Vogler et al. (11), equaling approximately 25% of patients before randomization. These patients were included in the original description of the technique, in which termination of AF by PVI alone was only achieved in 14%, again suggesting a more advanced AF phenotype in the original stepwise population compared with the current study.

That additional CFAE ablation does not confer a specific additional benefit should not be surprising; the underlying mechanisms of CFAEs are incompletely understood (26), and several different phenomena apparently can give rise to fractionated electrograms (27). Furthermore, the positive and negative predictive values of different qualities of CFAEs are little better than a coin toss (28).

FACTORS CRITICAL TO SUCCESS

The impressive overall AF termination rate in the study by Vogler et al., using PVI alone, highlights several important issues. Patient selection is clearly critical for achieving long-term technical and clinical success. Unfortunately, the noninvasive tools we use are fraught with their own limitations. Conversely, defining patients based on history and duration of AF appears simple, but in clinical practice is decidedly less so (13). Still, a noninvasive inverse potential mapping system, with limited availability at present, suggests that an important change occurs in the AF substrate in patients with persistent AF for 9 to 12 months, which affects the amount of ablation necessary to obtain a favorable rhythm outcome (29). Although cardiac magnetic resonance imaging (CMR) may categorize patients with a favorable versus a more unfavorable substrate (30), so far this has not seen widespread adoption. Various technical reasons may explain why (31), ranging from technical facets of the CMR process to the exact histological characteristics of fibrosis being assessed (32).

Procedural termination of AF is also somewhat controversial (5,8,15,16,18,19). Most studies suggest that procedural termination favors an improved longterm outcome from AF ablation and independently predicts success, although the magnitude can vary from a hazard ratio of 1.28 (19) to 3.8 (16) at 5 years. Procedural termination of an arrhythmia has been considered the gold standard from the early days of radiofrequency ablation, when the mechanism of arrhythmias seemed well understood. The problem with AF is that currently the underlying mechanisms are incompletely understood; therefore, although termination may be the gold standard endpoint, Download English Version:

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