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EDITORIAL COMMENT

Ablation of persistent atrial fibrillation: Pursuing different strategies for treating a progressive disease

Ablação de fibrilhação auricular persistente: diferentes estratégias para o tratamento de uma doença progressiva

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The first attempts to eliminate atrial fibrillation (AF) were originally made in 1987 by James Cox, who described the 'maze' procedure, which involved open-heart surgery with a cut-and-sew technique.[1] Although it achieved a good success rate, major postoperative complications occurring in a significant proportion of patients limited the expansion of the procedure. In 1998 Michel Haïssaguerre reported the ablation of paroxysmal AF triggers within the pulmonary veins (PVs).[2] With time, percutaneous catheter ablation of AF has consistently demonstrated to be a much safer approach and circumferential isolation of the PVs using point-by-point radiofrequency ablation or single-shot ablation techniques became the cornerstone of ablative therapy.

Despite enormous progress in recent decades, with improvement in scientific knowledge, refinement of three-dimensional mapping systems, the development of highly efficient catheters and deflectable sheaths, new forms of energy, contact force sensing catheters and, more recently, indices of lesion creation prediction, some issues remained unresolved, such as rates of PV reconnection as high as 70%[3] and a significantly lower success rate in ablation of persistent compared to paroxysmal AF.

In paroxysmal AF, 70-90% of AF triggers originate in or around the PVs, but in persistent AF significant electrical and structural remodeling of the atria occurs and non-PV foci may be more prevalent. A substantially higher recurrence rate after PV isolation supported the concept that this technique alone may be insufficient in catheter ablation of persistent AF in some patients, and more extensive atrial ablation has been advocated including additional linear ablation, complex fractionated atrial electrogram (CFAE) ablation, rotor ablation, cardiac autonomic denervation, isolation of the superior vena cava or the left atrial appendage, and extra-PV foci ablation. Additional benefit justifying the use of such techniques in a first procedure is yet to be confirmed. The STAR AF II trial and several other smaller prospective trials compared some of these strategies and documented no incremental benefit of additional left atrial ablation compared to PV isolation alone in patients with persistent AF, with 59% of patients assigned to PV isolation alone free from AF recurrence at 18 months follow-up.[4] The reasons for this lack of benefit are unclear. One possible explanation is that more extensive ablation generates more scar in an already diseased left atrium (and also increases the risk of complications). Extensive atrial scarring has been directly linked to increased AF recurrence rate,[5] so limited ablation and balanced substrate modification are essential for achieving a better long-term outcome. Targeting extra PV foci and selective ablation of low-voltage areas as an adjunct to PV isolation have shown improved outcomes in randomized trials involving a smaller number of patients.[6]

In the current issue of the *Journal*, Freitas et al.[7] present a retrospective analysis of 67 consecutive patients referred to a tertiary center for catheter ablation of persistent (60%) or long-standing persistent (40%) AF over a period of 30

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months. In the first 14 months (group 1: 27 patients), circumferential PV isolation plus CFAE ablation were performed. In the subsequent 16 months (group 2: 40 patients), a tailored approach including PV isolation, tissue homogenization of low-voltage areas, creation of lines connecting areas of scar and CFAE ablation was the strategy adopted. Isolated circumferential PV isolation was performed in only 30% of patients in both groups. In a mean follow-up of 16±6 months, arrhythmia recurrence was observed in 40.7% of patients in group 1, while with the tailored approach AF recurred in only 17.5%.

The main limitations of this study are acknowledged by the authors in the discussion: the number of patients was relatively small and, most importantly, the different strategies were undertaken at different times, which led to improvements in operator experience and the development of important technological tools that occurred during the study period, particularly the availability of indices of lesion creation prediction that enable more durable lesions and sustainable PV isolation. As their introduction into clinical practice was more recent, only group 2 patients were able to benefit from this technology, which may have had a major impact on the results. The tailored approach proposed by Freitas et al. showed excellent results and has the merit of aiming to select patients who apparently do not qualify for additional ablation beyond PV isolation, avoiding more extensive ablation. The main limitation of this tailored approach is that many of the associated ablation techniques are to a large degree operator-dependent: there is significant subjectivity involved (particularly in CFAE analysis), and achieving and validating bidirectional linear block is difficult and not always accurate even with experienced operators. Some of these issues may explain why the results of most of these techniques employed in similar studies are difficult to reproduce in multicenter clinical trials. Nevertheless, it seems reasonable to conclude from the available data that in a significant proportion of patients with persistent AF, circumferential PV isolation by itself will not be sufficient and additional targets will have to be selected.

Similarly to coronary artery disease, persistent AF is a progressive illness, one in which catheter ablation alone has a significant rate of arrhythmia recurrence at five years follow-up, and lifestyle modifications (like reduction of weight and alcohol consumption), medical therapy and other therapies yet to be developed may be needed to maintain sinus rhythm in the long term.

Over the coming years, indices of lesion formation and new energy sources such as pulse-field ablation promise to achieve durable PV isolation, which will enable assessment of the true efficacy of isolated PV isolation, the actual need for additional targets in some patients, and the best way to tailor this approach using an evidence-based methodology. This being said, ablation of low-voltage areas may be a promising technique.

Meanwhile, catheter ablation of persistent AF has consistently demonstrated reasonable efficacy, a significant reduction in the number and duration of AF episodes (AF burden),[8,9] improvement of patient symptoms and reduced mortality, particularly in patients with heart failure.[10]

Conflicts of interest

The author has no conflicts of interest to declare.

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