

## GUEST EDITOR'S PAGE



# First-Line Approach for Rhythm Control in Paroxysmal Atrial Fibrillation



## Which Is the Optimal Treatment?

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**A**trial fibrillation (AF) is the most common arrhythmia worldwide, affecting approximately 1% to 2% of the overall population. Patients with AF report a significant deterioration in their quality of life (QoL) because of the symptoms related to the arrhythmia, but also to the increased risk for the development of organ complications (heart failure, stroke, cardiac death).

The primary indication for rhythm control (restore and maintain sinus rhythm) is to reduce AF-related symptoms and improve QoL.<sup>1</sup> The recent EAST-AFNET 4 trial (Early Treatment of Atrial Fibrillation for Stroke Prevention Trial) showed that early rhythm control is superior to usual care in improving cardiovascular outcomes at the 5-years follow-up visit.<sup>2</sup> Guidelines currently recommend the initial use of antiarrhythmic drugs (AADs) for the maintenance of sinus rhythm.<sup>1,3</sup> However, the efficacy of first-line AADs therapy is limited because of their deleterious side effects, such as proarrhythmia and organ toxicity, resulting in a substantial proportion of patients discontinuing therapy. Pulmonary vein isolation (PVI) catheter ablation is a well-accepted strategy for long-term rhythm control, emerging as a first-line

treatment in patients with paroxysmal AF. Nevertheless, the American and European guidelines provide a conditional recommendation in Class IIB patients for the former and in Class IIa patients for the latter as first-line therapy.<sup>1,3</sup> Initial randomized clinical trials (RCTs) comparing radiofrequency catheter ablation with AADs as first-line therapy for paroxysmal AF reported a significant lower risk of AF recurrence in the ablation group, with a modest incidence of complications.<sup>4,5</sup> These data should be interpreted in the context of heterogeneity in the procedural endpoints and procedural workflow. Moreover, the results were also limited by intermittent rhythm monitoring, high rates of crossover from AADs to ablation, and high rates of repeated ablation procedures.

Recently, 3 similar multicenter RCTs, assessing Cryoballoon catheter ablation versus AADs in patients with symptomatic, not treated, paroxysmal AF reported a reduction in recurrence of atrial arrhythmias and hospitalizations, with no difference in major adverse events.<sup>6-8</sup> The 3 studies, the Cryo-FIRST (Catheter Cryoablation Versus Antiarrhythmic Drug as First-Line Therapy of Paroxysmal Atrial Fibrillation),<sup>6</sup> the EARLY-AF (Early Aggressive Invasive Intervention for Atrial Fibrillation),<sup>7</sup> and the STOP-AF (Cryoballoon Catheter Ablation in an Antiarrhythmic Drug Naive Paroxysmal Atrial Fibrillation)<sup>8</sup> trial, included a total of 724 patients who were followed up for 12 months. Most of the patients enrolled were relatively free of significant comorbidities, and the mean age of populations among the studies was 57.4 years. In addition to demonstrating a reduction in atrial tachyarrhythmia

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recurrence, compared with AADs, an improvement in the QoL was reported. In particular, in the Cryo-FIRST and the EARLY-AF trials, the authors reported that patients treated with initial ablation were significantly more likely to be symptom free at their follow-up visits.

In a recent systematic review and meta-analysis<sup>9</sup> evaluating the safety and efficacy of AF ablation as first-line therapy when compared with AADs in patients with paroxysmal AF, 6 RCTs were included. The study involved 1,212 patients with paroxysmal AF, treated with both radiofrequency and Cryoballoon ablation.

The analysis concluded that catheter ablation was associated with a 38% reduction in atrial arrhythmias and a 68% reduction in hospitalizations compared with AADs. Moreover, no difference in major adverse events between groups was found.

The reduction in hospitalizations and the improvement in QoL may significantly reduce healthcare use and costs. This is not neglectable, inasmuch as AF direct costs for hospitalizations and acute care are thought to increase approximately 1.0% to 4% within the next 2 decades.

Based on these premises, a paradigm shift in the current guidelines is eagerly awaited. Indeed, data suggest that PVI might be considered as first-line rhythm control therapy in patients with paroxysmal AF. Furthermore, the time between a first episode of AF and catheter ablation matters. In the EAST-AFNET 4, only early rhythm control (eg, <1 year from AF first diagnosis) has demonstrated to improve hard endpoints. In this study, approximately 19% of patients underwent catheter ablation as a rhythm control strategy during 2 years follow-up. Catheter ablation, leading to fewer recurrences compared with AADs, might improve the long-term clinical outcomes if used early.

Indeed, the time between AF diagnosis and ablation is a known predictor of recurrence.

Nevertheless, patients with AF have often other cardiovascular and noncardiovascular comorbidities, which have been linked to the progression and recurrence of the arrhythmia. In this regard, a holistic approach to management is recommended, considering coexisting diseases and lifestyle changes. Therefore, although with suboptimal efficacy, AADs may be a reasonable option in selected patients as a first-line therapy to prepare the patient for the ablation procedure or in patients for whom ablation is deemed contraindicated.

Thus, patient selection and multidisciplinary teamwork are mandatory in AF workflow. Catheter ablation as a first-line approach for paroxysmal atrial fibrillation can be effective only if both the patient and the cardiologist are involved in a shared and evidence-based pathway.

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