

Cryoballoon in persistent atrial fibrillation: a standardized or individualized approach?

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Catheter ablation has been shown to be superior to medical treatment for the maintenance of sinus rhythm in patients with atrial fibrillation (AF) and refractory symptoms. Pulmonary vein isolation (PVI) is the cornerstone of catheter ablation for AF. Patients with persistent AF are more prone to recurrences due to electrical and structural remodeling.

The use of cryoballoon (CB) ablation for PVI has substantially increased in recent years. The FIRE AND ICE trial, which prospectively randomized patients with paroxysmal AF to either radiofrequency (RF)- or CB-based PVI, showed that these 2 methods have similar efficacy and safety in the treatment of paroxysmal AF.¹ Furthermore, evidence indicates that PVI alone is not inferior to additional substrate modification in patients with paroxysmal or persistent AF.² In patients with long-standing persistent AF, there were no significant differences when a PVI-only approach was compared with a stepwise method of PVI plus linear and complex fractionated electrograms. A multi-center study then reported that CB ablation of pulmonary veins was safe, effective, and efficient for the treatment of patients with persistent and long-standing persistent AF.³ Finally, a recent multinational European study compared second-generation CB versus conventional irrigated-tip RF in a real-world mixed population of patients with paroxysmal and persistent AF. CB ablation was found to have shorter procedure times compared with RF, irrespective of the ablation lesion set used for the treatment of AF. The complication rates were low and did not differ between groups. The result was not influenced by the AF type or the lesion sets applied, and freedom from

arrhythmia recurrence did not differ between the CB and the RF groups.⁴ Information such as this has facilitated the expansion of the indications for CB ablation to patients with persistent AF.

In this issue of *Kardiologia Polska (Kardiol Pol, Polish Heart Journal)*, Liu et al⁵ conducted a meta-analysis, including a total of 7 studies, aiming to compare the role of CB ablation with RF ablation in persistent AF. The findings suggested that success rates and procedural complications were comparable between the groups. There were no differences in freedom from atrial arrhythmia, procedural complications, AF/AT relapse during the blanking period, repeat ablation, and vascular complications. A subanalysis of the meta-analysis showed a lower incidence of recurrent atrial arrhythmia and repeat ablation during CB ablation without touch-up RF ablation in PVI. Based on the findings, Liu et al⁵ suggested that CB ablation alone could provide an alternative technique for ablation in persistent AF.

The main limitation of this meta-analysis is the heterogeneity of technology employed in the studies. Second-generation CB ablation was used in most studies, except in the study performed by Boveda et al,⁶ where first-generation CB ablation was employed. On the RF side, only 3 studies included the use of contact force (CF)-guided ablation.^{7,8} The subanalysis showed that patients in the RF ablation with CF group had a lower incidence of repeat ablation. CF catheters provide information to the operator to assess the proximity of the catheter to the endocardium. Low CF during PVI is a predictor of acute and chronic pulmonary vein reconnections and

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is associated with an increased risk of AF recurrence. Newer CF-guided techniques use target indices for ablation (such as the “ablation index”) that combine CF, power, and time to determine when an optimal lesion has been delivered. The CLOSE protocol, for example, is an ablation protocol guided by an ablation index aimed at isolating the veins with stable, contiguous, and optimized CF RF ablation.⁹ With this technique, 62% of repeat patients had complete, durable isolation, which confirms that RF protocols like CLOSE can improve outcomes by avoiding weak links in the ablation chain.¹⁰

The other major limitation is the heterogeneity of ablation techniques used among the studies, but even between the CB and RF arms within studies. Five studies allowed for RF touch-up in addition to CB. In 4 studies, cross-over allowed additional lines, such as the cavotricuspid isthmus flutter line, to be performed with RF in the CB group. In 2 studies, the CB strategy was limited to PVI, while the RF strategy allowed for extensive ablation beyond PVI including complex fractionated electrograms, lines, and posterior wall isolation. With all of these different strategies, it is very difficult to tell how much of the benefit was conferred by the technology versus the approach to ablation. The STAR AF II trial, for example, found that catheter ablation of complex fractionated electrograms and linear ablation, in addition to PVI, did not improve the rate of recurrent AF.² In fact, such additional ablation seemed to worsen the outcome, which may have biased against the RF strategies in the current meta-analysis. Furthermore, if an RF catheter has to be employed for touch-up or additional linear ablation in the CB group, then can a CB strategy really be considered an alternative given the added cost of including an RF catheter as well?

The results of 2 previous meta-analyses¹¹ on this topic are in line with the meta-analysis conducted by Liu et al⁵; however, it is hard to conclusively say that CB ablation is superior or non-inferior to RF ablation in patients with persistent AF due to several other limitations, such as nonrandomized patient selection, relatively small sample size of the studies, and less extensive postablation rhythm monitoring than other leading centers, which might underestimate the rate of AF recurrence after ablation.

The current meta-analysis⁵ also did not include any studies of CB ablation in patients with impaired left ventricular function. Until now, there is only 1 study showing an acceptable AF recurrence-free rate at year 1 in patients with low ejection fraction, which reported that AF recurrence-free individuals were more likely to have improved ejection fraction.¹² However, more data is needed in this group of patients.

Furthermore, RF technology continues to evolve. A new game-changer in the catheter

ablation of AF is the implementation of the so-called “high-power and short-duration” RF ablation, which has shown to provide a higher success rate with fewer complications and shorter procedure duration.¹³

The techniques for ablation of persistent AF also continue to evolve. We acknowledge that PVI, per se, may not be sufficient in patients with persistent AF due to the progressive nature of the disease. Sustained AF results in electrical, contractile, and structural remodeling, particularly in patients with persistent AF. Several studies have shown that approximately a third of AF triggers in persistent AF are found to be non-pulmonary venous. The most common sites are the superior vena cava, ligament of Marshall, coronary sinus, crista terminalis, left atrial posterior wall, and left atrial appendage (LAA).² We know that RF ablation with a point-by-point catheter and mapping system facilitates the creation of non-pulmonary venous lesions in both atria, so if more than PVI is required for persistent AF ablation, then the advantage may decidedly speak in favor of RF. However, CB is now increasingly being used to create non-pulmonary venous lesions as well. Yorgun et al¹⁴ showed that LAA isolation with CB as an adjunct to PVI improves long-term freedom from AF recurrence compared with the PVI-only strategy in persistent AF. In addition to LAA isolation with CB ablation, another study demonstrated the feasibility of CB ablation in posterior wall isolation with improved 1-year freedom rate from atrial arrhythmia in patients with persistent AF.¹⁵ Newer developments in CB technology, such as more malleable balloons with varying shapes, may also facilitate ablation beyond the pulmonary veins.

Two new ongoing randomized studies will hopefully provide more promising data regarding the efficacy and safety of CB versus RF ablation in patients with persistent AF. FIRE AND ICE II Trial Pilot (ClinicalTrials.gov identifier, NCT03706677) is the pilot phase of a prospective, randomized, single-blinded, multicenter, interventional postmarket clinical trial comparing the efficacy and safety of isolation of the pulmonary veins using a CB catheter or RF ablation with a ThermoCool Smarttouch catheter in patients with persistent AF. Another ongoing randomized study is aimed to compare PVI with the CB and RF energy (CF) in the treatment of persistent AF (ClinicalTrials.gov identifier, NCT03053570).

In conclusion, regardless of the preferred energy source, both CB and RF ablation can safely achieve reasonable success in the treatment of persistent AF. The optimal ablation strategy and technology for patients with persistent AF is still unknown, and probably an individualized interventional approach in patients with persistent AF will be required.

ARTICLE INFORMATION

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