



Editorial

Light and shadows of atrial fibrillation ablation using a cryoballoon☆

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In 1998, Haissaguerre et al. reported that ectopy originating from the pulmonary veins (PVs) initiated atrial fibrillation (Afib) and that radiofrequency (RF) ablation at the site of the ectopic focus reduced the likelihood of an Afib recurrence [1]. The ectopic foci in the PVs can also be treated by electrical isolation of the veins from the left atrium (LA) at the LA-PV junction. Several clinical trials have demonstrated that ablation success rates at 12 months are generally in the 60–75% range. Therefore, RF ablation can provide favorable effects for patients with symptomatic Afib. According to the 2012 Japanese guidelines for indications and procedural techniques of catheter ablation, catheter ablation of drug refractory paroxysmal Afib is a class I indication and electrical isolation of the PVs is the standard approach.

While, Afib is a significant risk factor for thromboembolic strokes, it also increases the total mortality. Whether ablation prevents strokes or prolongs life is uncertain. Several non-randomized follow-up studies have reported favorable outcomes for ablated patients. However, the RF ablation used in these trials requires time-consuming point-to-point delivery of multiple applications to isolate the PVs, and this approach demands extensive training. This complexity has restricted the ablation therapy for Afib to a few specialized centers and has limited the availability of the ablation.

The cryoballoon has been developed and tested as an alternative, single-delivery approach to the isolation of the PVs. It has been suggested that cryoballoon ablation might have the potential to overcome the complexity of RF ablation. The STOP AF trial was the first trial in a randomized fashion to clarify the safety and efficacy of cryoballoon ablation as compared to drug therapy [2]. The FIRE AND ICE trial demonstrated the noninferiority of cryoballoon ablation targeting paroxysmal Afib regarding the effectiveness and safety as compared to RF ablation [3]. Furthermore, the mean total procedure time was shorter in the cryoballoon group than in the RF group (124 vs. 141 min,

$p < 0.001$), as was the LA dwell time (92 vs. 109 min, $p < 0.001$). In this trial patients treated with a second-generation cryoballoon had significantly fewer redo procedures during the follow-up than those treated with RF ablation [4]. Recently, the long-term outcomes based on the ESC-EHRA atrial fibrillation ablation registry and Swedish catheter ablation registry have been published [5]. With regard to the freedom from arrhythmia recurrence there was no difference between the cryoballoon and RF ablation groups. Further, the procedural duration was significantly shorter in the cryoballoon group than RF group. Furthermore, the re-ablation rate after 12 months was significantly lower for the cryoballoon (7.8%) versus RF (11%, $p = 0.005$). These results are in accordance with those of the FIRE AND ICE trial. Therefore, presently the efficacy and safety of cryoballoon ablation for paroxysmal Afib seems to be widely accepted.

Several types of complications concerning cryoballoon ablation have been reported. According to Rottner et al. [6], procedure-related complications were comparable between the cryoballoon and RF ablation groups. However, cryoballoon ablation led to higher rates of phrenic nerve palsy (2.7%). Moertsell et al. also reported a higher incidence of phrenic nerve palsy in the cryoballoon ablation group, while there was a lesser incidence of pericarditis [5]. Further, the incidence of other complications, such as gastrointestinal, neurological, peripheral vascular, and pulmonary event-related complications, was comparable. PV stenosis is one of the complications after Afib ablation. A reduction in the PV dimension is often observed even after cryoballoon ablation. A larger PV ostium and lower minimum freezing temperature during cryoballoon ablation have been associated with an increased risk of a PV dimension reduction [7]. This might suggest that larger-sized PVs are not optimal candidates for cryoballoon ablation.

In the current issue of the *Journal of Cardiology*, Lyan et al. [8] report a series of atrial tachycardias (ATs) post Afib ablation using the second-generation cryoballoon. Regular ATs are known to be one of the complications and have been well documented. ATs post Afib ablation are less prevalent after cryoballoon ablation in comparison to RF ablation [9–11]. This is probably because the cryothermal energy can create homogenous and well-demarcated lesions at the PV-LA junction. The prevalence of ATs reported by previous studies are 6% [10], 3% [11], 9.2% [12], and 8% [13], while the current study [8] reported a prevalence of 11.3%. Potential explanations for the differences in the prevalence of ATs might be the heterogeneity of the study populations, with a higher prevalence of persistent Afib (61.8%) in the current study compared to the other studies. The advancement of remodeling of the atrial

myocardium may be more prominent in persistent Afib than paroxysmal Afib, and thus may result in fibrotic changes of the atrial myocardium and provide the substrate for macroreentry. Two mechanisms can produce ATs after Afib ablation, focal activity related to PV reconnections and macroreentry in the LA. The prevailing mechanism of AT is macroreentry (24/26 patients), including common atrial flutter (10 patients) in the current study [8]. This is the first report systematically analyzing voltage maps of ATs post cryoballoon ablation. Interestingly, all bipolar voltage maps of left ATs have revealed the presence of abnormal low voltage areas (>0.5 mV), which can play a role as a slow conduction isthmus for macroreentry.

The effectiveness of cryoballoon ablation for paroxysmal Afib is generally accepted because of the 'light side' of the cryoballoon ablation. One of the existing topics is the effectiveness of the cryoballoon for persistent Afib. Several studies concerning this issue have already been published and others are still ongoing. This study revealed one of the 'shadow sides' of the cryoballoon ablation, such as a high occurrence rate and the mechanism of ATs after cryoballoon ablation of persistent Afib. Therefore, this study might provide a clue to the decision of the strategy for Afib ablation.

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References

- [1] Haissaguerre M, Jais P, Shah DC, Takahashi A, Hocini M, Quiniou G, et al. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. *N Engl J Med* 1998;339:659–66.
- [2] Packer DL, Kowal RC, Wheelan KR, Irwin JM, Champagne J, Guerra PG, et al. Cryoballoon ablation of pulmonary veins for paroxysmal atrial fibrillation First results of the North American Arctic Front (STOP AF) pivotal trial. *J Am Coll Cardiol* 2013;61:1713–23.
- [3] Kuck KH, Brugada J, Fuernkranz A, Metzner A, Ouyang F, Chun KRJ, et al. Cryoballoon or radiofrequency ablation for paroxysmal atrial fibrillation. *N Engl J Med* 2016;374:2235–45.
- [4] Kuck K-H, Fuernkranz A, Chun KRJ, Metzner A, Ouyang F, Schlueter M, et al. Cryoballoon or radiofrequency ablation for symptomatic paroxysmal atrial fibrillation: reintervention, rehospitalization, and quality-of-life outcomes in the FIRE AND ICE trial. *Eur Heart J* 2016;37:2858–65.
- [5] Moertzell D, Arbelo E, Dagres N, Brugada J, Laroche C, Trines SA, et al. Cryoballoon vs. radiofrequency ablation for atrial fibrillation: a study of outcome and safety based on the ESCV-EHRA atrial fibrillation ablation long-term registry and the Swedish catheter ablation registry. *Europace* 2018. <http://dx.doi.org/10.1093/europace/euy239>.
- [6] Rottner L, Fink T, Heeger CH, Schlueter M, Goldmann B, Lemes C, et al. Is less more? Impact of different ablation protocols on periprocedural complications in second-generation cryoballoon based pulmonary vein isolation. *Europace* 2018;20:1459–67.
- [7] Narui R, Tokuda M, Matsushima M, Isogai R, Tokutake K, Yokoyama K, et al. Incidence and factors associated with the occurrence of pulmonary vein narrowing after cryoballoon ablation. *Circ Arrhythm Electrophysiol* 2017;10. pii:e004588.
- [8] Lyan E, Yalin K, Abdin A, Sawan N, Liosis S, Lange SA, et al. Mechanism, underlying substrate and predictors of atrial tachycardia following atrial fibrillation ablation using the second-generation cryoballoon. *J Cardiol* 2019;73:496–507.
- [9] Cardoso R, Mendirichaga R, Fernandes G, Healy C, Lambrakos LK, Viles-Gonzalez JF, et al. Cryoballoon versus radiofrequency catheter ablation in atrial fibrillation: a meta-analysis. *J Cardiovasc Electrophysiol* 2016;27:1151–9.
- [10] Akerström F, Bastani H, Insulander P, Schwieler J, Arias MA, Jensen-Urstad M. Comparison of regular atrial tachycardia incidence after circumferential radiofrequency versus cryoballoon pulmonary vein isolation in real-life practice. *J Cardiovasc Electrophysiol* 2014;25:948–52.
- [11] Juliá J, Chierchia GB, de Asmundis C, Mugnai G, Sieira J, Ciconte G, et al. Regular atrial tachycardias following pulmonary vein isolation for paroxysmal atrial fibrillation: a retrospective comparison between the cryoballoon and conventional focal tip radiofrequency techniques. *J Interv Card Electrophysiol* 2015;42:161–9.
- [12] Hermida A, Kubala M, Traullé S, Buiciuc O, Quenum S, Hermida J-S. Prevalence and predictive factors of left atrial tachycardia occurring after second-generation cryoballoon ablation of atrial fibrillation. *J Cardiovasc Electrophysiol* 2018;29:46–54.
- [13] Mikhaylov EN, Bhagwandien R, Janse PA, Theuns DAMJ, Szili-Torok T. Regular atrial tachycardias developing after cryoballoon pulmonary vein isolation: incidence, characteristics, and predictors. *Europace* 2013;15:1710–7.

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