



EDITORIAL COMMENT

Standardizing atrial fibrillation ablation with the cryoballoon: A song of ice versus fire?



Normalizar a ablação da fibrilhação auricular com criobalão: o Gelo versus o Fogo?

João Primo^{a,b,*}, Sérgio Barra^{a,b,c}

^a Cardiology Department, V. N. Gaia Hospital Center, Vila Nova de Gaia, Portugal

^b Cardiology Department, Hospital da Luz Arrábida, Vila Nova de Gaia, Portugal

^c Cardiology Department, Royal Papworth Hospital NHS Foundation Trust, Cambridge, UK

There is increasing interest in single-shot techniques for the electrical isolation of the pulmonary veins in patients with atrial fibrillation (AF). Ablation using the cryoballoon is the most widely performed single-shot technique for AF ablation, although other techniques and equipment are also available. To date, equipment for cryoballoon ablation has been provided by one manufacturer only, but in the near future cryoablation with new balloon-type catheters or using alternative sources of energy (radiofrequency or lasers, for example) will be made available by other manufacturers.

Several factors have contributed to the increasing interest in single-shot techniques. Firstly, it is known that the incidence and prevalence of AF are significantly higher than initially thought, particularly in its paroxysmal form.¹ This is the likely result of the aging of the population and increasing prevalence of age-related conditions associated with AF, such as hypertension, diabetes and sleep apnea. Secondly, common sense dictates that the longer the monitoring period the higher the likelihood of finding AF,² and therefore with better and more prolonged screening methods, more patients can be expected to be diagnosed with the condition. Thirdly, although AF prevalence increases with

age, physicians are increasingly required to treat younger patients for whom chronic antiarrhythmic therapy is not an attractive option. Except for beta-blockers and calcium channel blockers, which have only modest efficacy for AF control, the long-term safety of antiarrhythmic drugs is questionable at best.

Early diagnosis and treatment of patients with AF, which includes risk factor modification, catheter ablation and anticoagulation when indicated, affects not only arrhythmia burden and quality of life, but also associated morbidity and mortality. This is particularly important for specific subgroups of patients such as those with heart failure and left ventricular systolic dysfunction, who may derive prognostic benefit from AF ablation.^{3,4} In a subanalysis of the Randomized Evaluation of Long-Term Anticoagulant Therapy (RE-LY) trial, only around 7% of deaths among anticoagulated AF patients were due to stroke or peripheral embolism, with most deaths resulting from other cardiac causes or non-cardiovascular conditions.⁵ This highlights the efficacy of anticoagulation and adjuvant treatments in the prevention of stroke. As patients on adequate anticoagulation are already at very low risk of cardioembolic stroke, and given the lack of temporal relationship between episodes of AF and stroke, future discussion should focus on the issue of mortality reduction as an important goal of AF treatment.⁶ In the recently published CABANA trial, intention-to-treat analysis showed no prognostic benefit of ablation compared with antiarrhythmic drugs, although the as-treated and per-

DOI of original article:

<https://doi.org/10.1016/j.repc.2019.05.013>

* Corresponding author.

E-mail address: joaojoseprimo@gmail.com (J. Primo).

protocol analyses suggested a benefit for those who were actually treated.⁷ Importantly, the subanalysis on patients with heart failure did show a strong trend for prognostic benefit of ablation, even in the intention-to-treat analysis.³ The question of whether AF ablation may also reduce the long-term risk of dementia is also worthy of further research. In summary, AF patients should be diagnosed and treated at an earlier stage of their condition, preferably with a more efficacious treatment such as catheter ablation, in order to reduce the morbidity and potentially the mortality associated with AF. The reduction of stroke risk is undoubtedly an important goal but this may be achieved with anticoagulation if indicated by the patient's CHA₂DS₂-VASc score, as well as with risk factor modification.

To accomplish the objective of reducing the overall epidemiological burden of AF and associated morbidity, it is paramount that the number of centers providing this treatment is increased, and that each center performs an increasing number of ablations per year. Cryoballoon ablation may be useful in this regard, enabling an increase in the overall number of cases given the faster learning curve even in less experienced centers and the similar success rates compared with radiofrequency ablation, a technique which is more dependent on operator experience.⁸

In this issue of the *Journal*, Elvira Ruiz et al. report medium- and long-term results of a single Medtronic second-generation cryoballoon (CB2)-based ablation procedure in patients with paroxysmal and persistent AF.⁹ All patients who underwent a first ablation procedure for AF using the CB2 technique in this single tertiary center between June 2012 and June 2017 were retrospectively analyzed. A total of 172 patients (134 with paroxysmal and 38 with persistent AF) were included and acute success was achieved in the vast majority. After a median follow-up of 27 months, 58.1% of patients remained free of atrial arrhythmias (64.2% and 36.8% for paroxysmal and persistent AF, respectively). Left atrial size and clinical presentation as persistent (compared with paroxysmal) AF were predictors of recurrence, as expected.⁹

This study, carried out in a relatively small-volume center which performs 50-70 AF ablations per year, including 35 with the cryoballoon, nicely illustrates the notion that effective and safe cryoballoon AF ablation can be performed even in small centers. In fact, results and complication rates were in line with those seen in higher-volume hospitals.¹⁰ A previous study involving Portuguese hospitals and a higher number of patients showed very similar results.¹¹ Still, the faster learning curve of cryoballoon AF ablation should be weighed against the more precise point-by-point ablation achieved with radiofrequency contact-force catheters, particularly in an era where the extent and transmuralty of the ablation can be estimated with great precision with software such as Ablation Index (Biosense Webster, Inc). The present study further confirmed what multiple investigators have already shown: left atrial size and type of AF clearly impact the outcome. The retrospective nature of this study is of course its main limitation, and it is likely that some AF episodes may have been missed. Nevertheless, AF recurrence may not be as clinically relevant if episodes are of short duration, and the patient is asymptomatic and on adequate anticoagulation if indicated.

In conclusion, assuming the cryoballoon is non-inferior to other current techniques, as previous studies have suggested,^{12,13} AF ablation with this technology enables AF treatment to be widened with similar outcomes to the more traditional point-by-point radiofrequency ablation, a welcome benefit in an era in which the demand for AF treatment is rapidly increasing.

Conflicts of interest

The authors have no conflicts of interest to declare.

References

1. Primo J, Gonçalves H, Macedo A, et al. Prevalence of paroxysmal atrial fibrillation in a population assessed by continuous 24-hour monitoring. *Rev Port Cardiol.* 2017;36:535-46.
2. Roche F, Gaspoz JM, Da Costa A, et al. Frequent and prolonged asymptomatic episodes of paroxysmal atrial fibrillation revealed by automatic long-term event recorders in patients with a negative 24-hour Holter. *Pacing Clin Electrophysiol.* 2002;25:1587-93.
3. Marrouche NF, Brachmann J, Andresen D, et al. CASTLE-AF Investigators. Catheter ablation for atrial fibrillation with heart failure. *N Engl J Med.* 2018;378:417-27.
4. Di Biase L, Mohanty P, Mohanty S, et al. Ablation versus amiodarone for treatment of persistent atrial fibrillation in patients with congestive heart failure and an implanted device: results from the AATAC Multicenter Randomized Trial. *Circulation.* 2016;133:1637-44.
5. Marijon E, Le Heuzey JY, Connolly S, et al. RE-LY Investigators. Causes of death and influencing factors in patients with atrial fibrillation: a competing-risk analysis from the randomized evaluation of long-term anticoagulant therapy study. *Circulation.* 2013;128:2192-201.
6. Barra S, Narayanan K, Boveda S, et al. Atrial fibrillation ablation and reduction of stroke events: understanding the paradoxical lack of evidence. *Stroke.* 2019;50:2970-6. Epub 2019 Sep 12.
7. Packer DL, Mark DB, Robb RA, et al., CABANA Investigators. Effect of catheter ablation vs antiarrhythmic drug therapy on mortality, stroke, bleeding, and cardiac arrest among patients with atrial fibrillation: the CABANA Randomized Clinical Trial. *JAMA.* 2019;321:1261-74.
8. Providencia R, Defaye P, Lambiase PD, et al. Results from a multicentre comparison of cryoballoon vs. radiofrequency ablation for paroxysmal atrial fibrillation: is cryoablation more reproducible? *Europace.* 2017;19:48-57.
9. Ruiz GE, Verdú PP. Medium- and long-term outcome after a single second-generation cryoballoon ablation in patients with paroxysmal and persistent atrial fibrillation. *Rev Port Cardiol.* 2019;38, <https://doi.org/10.1016/j.repc.2019.05.013>.
10. Akkaya E, Berkowitsch A, Zaltsberg S, et al. Second-generation cryoballoon ablation for treatment of persistent atrial fibrillation: three-year outcome and predictors of recurrence after a single procedure. *J Cardiovasc Electrophysiol.* 2018;29:38-45.
11. Cunha PS, Fonseca P, Oliveira MM, et al. Clinical outcome after cryoballoon based pulmonary vein isolation for the treatment of paroxysmal and persistent atrial fibrillation: a two center experience. In: Abstract presented at the Portuguese Congress of Cardiology; 2019.
12. Boveda S, Providencia R, Albenque JP, et al. Real-time assessment of pulmonary vein disconnection during cryoablation of atrial fibrillation: can it be 'achieved' in almost all cases? *Europace.* 2014;16:826-33.
13. Kuck KH, Brugada J, Furnkranz A, et al. Cryoballoon or radiofrequency ablation for paroxysmal atrial fibrillation. *N Engl J Med.* 2016;374:2235-45.