



EDITORIAL COMMENT

Atrial fibrillation - How to improve prognosis and quality of life in 2021: Early ablation to stop atrial fibrillation and oral anticoagulation to avoid cardioembolic events



Fibrilhação auricular – Como melhorar o prognóstico e a qualidade de vida em 2021: ablação precoce para manter o ritmo sinusal e anticoagulação oral para evitar os eventos cardioembólicos

Pedro Adragão

Serviço de Cardiologia, CHLO, Hospital de Santa Cruz, Carnaxide, Portugal

Prevalence of atrial fibrillation

Atrial Fibrillation (AF) is the most frequent sustained arrhythmia in adults and a global pandemic which according to the most recent 2020 European Society of Cardiology (ESC) guidelines¹ affect 43 million people worldwide.

It is important to note that the graph showing the global prevalence of AF, reveals Portugal has a prevalence of <600 per 100 000 inhabitants. It is the only country in the European Union that has a similar pattern of incidence as observed on the African continent. Unfortunately, this graph, although chromatic, loses credibility when confronted with the lack of statistic accuracy, since according to the well-structured methodology of the FAMA study,² the real value is more than 1250 per 100 000 inhabitants. This value is in line with data showing that the principal cause of mortality in Portugal is stroke. This places us among the countries with the greatest prevalence of AF (together with Scandinavia, Switzerland, Canada and the USA). Adjustments to the European guidelines are required to recognize the urgency, need for preventive measures and

therapeutics for AF. These measures should be implemented here in Portugal and supported by the European Union.

Natural history and prognostic impact

Atrial fibrillation is a disease that progresses from short and rare episodes to longer and more frequent ones. As the years pass, many patients develop persistent forms of AF, usually after the fourth decade of life and only a small percentage of patients will remain in paroxysmal AF (2-3%). Another aspect is that AF doubles mortality even under oral anticoagulation (OAC), as the incidence of stroke is of 1%/year and cardioembolic asymptomatic episodes lead to cognitive decline and dementia.¹ The main causes of death in patients with AF under OAC are stroke at 12% (6% ischemic and 6% hemorrhagic) and 30% cardiovascular (CV) events (heart failure [HF] and sudden death).

Atrial fibrillation: An Achilles' heel

There is a handicap in the therapeutic approach to AF – it is clearly preferable to have and maintain normal sinus rhythm (SR), however in most patients a strategy is prescribed to

E-mail address: padragao@gmail.com

maintain ventricular rate control. As a strategy to maintain SR, catheter ablation is preferred but usually not chosen as the first-line treatment, as antiarrhythmic pharmacological therapy remains the first choice. The reasoning behind this conflict between the strategy that we prefer and the one that we indicate to the patient has been in existence since the publication of the AFFIRM study.³ The strategy of controlling rhythm with antiarrhythmic drugs and non-systematic OAC overlaps with the strategy for ventricular rate control in AF maintaining systematic OAC.

In this study under analysis, it was found that only patients in SR and patients under OAC had prognostic benefits. Since then, the guidelines have indicated OAC and ventricular rate control as a first-line therapy without indication to maintain SR.

Cabana and Castle atrial fibrillation trials

To aggravate this contradictory situation, in 2019, the CABANA trial⁴ results were published. This trial compared catheter ablation with conventional pharmacological therapy. The results did not show any advantages of catheter ablation at reducing the primary endpoint (death+disabling stroke+hemorrhage+cardiac arrest). The Cabana trial showed a significant reduction in total mortality and CV hospitalization (secondary endpoint). Lack of compliance within the study protocol, which due to the crossover events, made its results inconclusive. A third of the patients in the pharmacological therapy arm underwent ablation anyway.

When analyzing the total mortality and disabling stroke we found that the group who underwent crossover for ablation was highly selected since it saw half of the deaths and strokes compared to the patients in the ablation arm, and three times less the number of episodes when compared to patients in the pharmacologic arm that did not undergo crossover.

In sum, the benefits of ablation in the intention-to-treat analysis were made null by the crossover rate. In fact, ablation reduced AF burden significantly, improved the patient's quality of life, had a small number of complications (similar to the pharmacological arm), and the per protocol evaluation showed a 32% reduction in total mortality (no crossover allowed).

These data confirm the previously obtained findings from patients with AF and HF in the CASTLE AF study a reduction of 51% in total mortality was observed.⁵

Atrial fibrillation guidelines 2020

Upon publication of these two major studies, the ESC guidelines from 2020¹ recommended that therapy should be patient-focused, with proactive monitoring of AF episodes, management of the CV risk, OAC according to the CHA₂DS₂-VASc score for the prevention of stroke, with the additional novelty that they had moved away from giving preference to the rate control strategy to placing it hand-to-hand with the strategy of maintaining SR. Nevertheless, it still does not recognize the prognostic advantage of maintaining SR.

The cornerstone of AF catheter ablation is pulmonary vein isolation that can currently be performed with point-

by-point radiofrequency (RF) or with a cryoablation balloon. Ablation is only indicated for symptomatic AF (paroxysmal/persistent). It is considered to be a class I indication after a relapse under antiarrhythmic drugs, and as a first option only if the patient has HF. It is a class IIa indication as a first-line approach for paroxysmal AF and class IIb for the persistent forms.

Early ablation to stop atrial fibrillation

In 2020, four different studies demonstrated the benefit of rhythm control, especially by ablation, after the appearance of AF episodes, which immediately leads us to question the AF guidelines bearing in mind the rationale of the above-mentioned indications.

It has been proven, for more than 10 years now, that early ablation of pulmonary veins with RF improves therapeutic success, reduces AF burden, improves quality of life, reduces CV hospitalization and avoids persistent AF progression.⁶⁻⁸ The guidelines have failed to fully reflect this therapeutic efficiency.

This year, a set of studies once again revealed what has already been demonstrated and came to similar conclusions.

The ATTEST study⁹ showed that ablation of paroxysmal AF patients with frequent episodes prevents its progression to persistent forms. RF ablation was far superior, when compared to antiarrhythmic drugs, at delaying progression to persistent AF after three years (2.4% progression versus 17.5%).

The EAST-AFNET 4¹⁰ study demonstrated that early rhythm control (AF for less than a year, median of 36 days), with drugs and/or ablation (8% at the start of the study, 19.4% at the end), significantly reduced the primary endpoint (CV mortality/stroke/hospitalization for CI+CAS) and preserves SR.

Two studies, EARLY AF¹¹ and STOP AF First,¹² which use cryoablation as a first-line treatment vs. pharmacologic therapy, were strongly in favor of ablation (75% of SR maintenance vs. 45%). These data confirm once again the need to readjust the guidelines to clinical reality.

Atrial fibrillation ablation and hard endpoints

In fact, for too long, major clinical records have shown the benefit of ablation by bringing about a clear reduction in mortality (CV and total), ischemic stroke and dementia. As commented in this editorial with regard to the CABANA study, ablation stands up to comparison with the main therapeutics indicated as class I in the cardiology guidelines.

For patients with AF and HF in the CASTLE study, treating nine patients was sufficient to save a life. In the CABANA trial, one life was saved in every 33 patients that underwent catheter ablation, and in the EARLY AF and STOP AF seven patients needed to be treated for one to be free from AF. These results should be compared with class I indication treatments as in the Aristotle study, 132 patients had to be treated with apixaban to save one life.¹³

Oral anticoagulation as a major step to improve atrial fibrillation outcome

Oral anticoagulation is an essential therapy in patients with AF to prevent cardio embolic events.¹

Non-vitamin K or direct oral anticoagulants (NOACs) were immediately introduced to the AF guidelines, which have since undergone constant updates. Their value is unquestionable and their adoption changed the prognosis and natural history of patients with AF, saving thousands of lives and also improving patient quality of life.

Optimizing prognosis in atrial fibrillation: A call to action in Portugal

This article published by Ferreira et al.¹⁴ sought to optimize the utilization of NOAC in Portugal. It is an exhaustive and detailed article in line with AF guidelines and explains how to manage OAC in our daily practice. Some items were guided by very recent scientific data, such as the use of NOACs during catheter ablation.

The strategy of not suspending NOAC is widely accepted, but it seems questionable to base the risk pattern on studies that could have patient selection bias and on those in which almost no hemorrhagic complications were found in the enrolled patients.

Maintaining OAC during percutaneous interventions should be assessed when thrombotic and/or hemorrhagic complications occur, and then the best option should be considered given the risk-benefit ratio for these major events. It is not only the rate of complications but also their severity and different solutions under effective or attenuated OAC.

In summary, “Early ablation to stop AF and oral anticoagulation to avoid cardioembolic events”. For the first time, the guidelines show what was already known: the rhythm maintenance strategy has never been inferior to the ventricular rate control strategy. Oral anticoagulation changed the natural history and the prognosis of AF and should be recommended and strictly implemented as indicated in AF guidelines. In 2021, studies have shown^{9–11} that for patients with AF, early rhythm control associated with judicious use of OAC has clinical and prognostic benefits, prevents evolution to persistent forms, improves quality of life and reduces mortality and CV hospitalizations.

We are born and prefer to live in sinus rhythm.

Conflicts of interest

The author has no conflicts of interest to declare.

References

- Hindricks G, Potpara T, Dagres N, et al., ESC Scientific Document Group. 2020 ESC guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J*. 2021;42:373–498.
- Bonhorst D, Mendes M, Adragão P, et al. Prevalence of atrial fibrillation in the Portuguese population aged 40 and over: the FAMA study. *Rev Port Cardiol*. 2010;29:331–50.
- Wyse DG, Waldo AL, DiMarco JP, et al. Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) Investigators. A comparison of rate control and rhythm control in patients with atrial fibrillation. *N Engl J Med*. 2002;347:1825–33.
- 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.
- 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.
- Pappone C, Radinovic A, Manguso F, et al. Atrial fibrillation progression and management: a 5-year prospective follow-up study. *Heart Rhythm*. 2008;5:1501–7.
- Wazni OM, Marrouche NF, Martin DO, et al. Radiofrequency ablation vs antiarrhythmic drugs as first-line treatment of symptomatic atrial fibrillation: a randomized trial. *JAMA*. 2005;293:2634–40.
- Cosedis Nielsen J, Johannessen A, Raatikainen P, et al. Radiofrequency ablation as initial therapy in paroxysmal atrial fibrillation. *N Engl J Med*. 2012;367:1587–95.
- Kuck KH, Lebedev DS, Mikhaylov EN, et al. Catheter ablation or medical therapy to delay progression of atrial fibrillation: the randomized controlled atrial fibrillation progression trial (ATTEST). *Europace*. 2020;(December):euaa298, <http://dx.doi.org/10.1093/europace/euaa298>. Epub ahead of print. PMID: 33330909.
- Kirchhof P, Camm AJ, Goette A, et al. EAST-AFNET 4 Trial Investigators. Early rhythm-control therapy in patients with atrial fibrillation. *N Engl J Med*. 2020;383:1305–16.
- Andrade JG, Wells GA, Deyell MW, et al. Cryoablation or drug therapy for initial treatment of atrial fibrillation. *N Engl J Med*. 2021;384:305–15.
- Wazni OM, Dandamudi G, Sood N, et al. STOP AF First Trial Investigators. Cryoballoon ablation as initial therapy for atrial fibrillation. *N Engl J Med*. 2021;384:316–24.
- Providencia R, Adragão P. Science deserves justice: the results of the CABANA trial are positive and support catheter ablation of atrial fibrillation for reducing mortality and hospitalizations. *Rev Port Cardiol*. 2019;38:245–50.
- Jorge Ferreira, Natália António, Nuno Cortez-Dias, et al. Optimizing prognosis in atrial fibrillation: a call to action in Portugal. *Rev Port Cardiol*. 2021;40.