

## Can We Consider Catheter Ablation as First-Line Therapy for all Our Atrial Fibrillation Patients Yet?

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### ABSTRACT

The prevalence of atrial fibrillation is increasing. Despite the well known prognostic benefits of maintaining sinus rhythm, pharmacological strategies have not provided satisfactory results showing limited efficacy, proarrhythmic effects, systemic toxicity and in some studies even increased mortality. AF ablation has undergone a great evolution with an increasing number of procedures performed all over the world. AF ablation is currently a topic of intense research. The results of recent research have raised catheter ablation indication as first-line therapy in patients with symptomatic paroxysmal AF in the 2012 focused update of the European Society of Cardiology guidelines. Although much effort remains to be done, we believe that technical evolution and the increasing expertise of teams performing ablation are allowing us to treat our patients with safer and more effective procedures. That is why AF ablation as first-line therapy is here to stay and probably we will be witness of a further extension of the indications.

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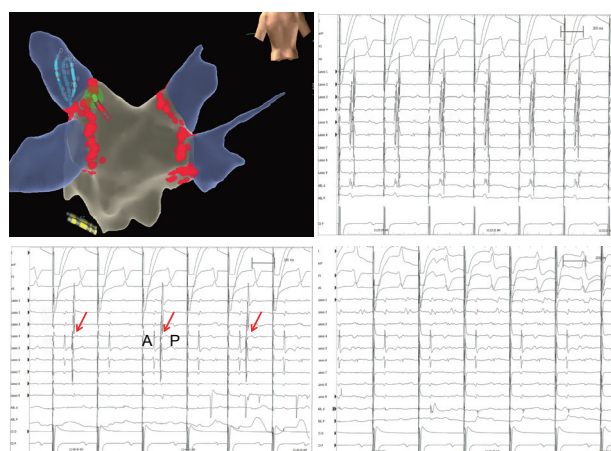
**Key words:** Atrial fibrillation; Catheter ablation

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### EDITORIAL

Epidemiological studies show that the prevalence of atrial fibrillation (AF) is increasing<sup>[1]</sup>. Despite the well known prognostic benefits of maintaining sinus rhythm, pharmacological strategies have not provided satisfactory results showing limited efficacy, proarrhythmic effects, systemic toxicity and in some studies even increased mortality<sup>[2]</sup>.

AF ablation has undergone a great evolution with an increasing number of procedures performed all over the world. Since its initial description in 1998, pulmonary vein ablation has been the cornerstone of AF ablation, specially for paroxysmal cases (Figure 1)<sup>[3]</sup>. In the last decade multiple randomized trials comparing treatment with catheter ablation with antiarrhythmic therapy have been published. Most of these studies have been conducted in patients with paroxysmal AF refractory to one or more antiarrhythmic drugs (AADs) and have shown that ablation is more effective than antiarrhythmic



**Figure 1** Electrical disconnection of the left superior pulmonary vein during a procedure of radiofrequency catheter ablation. In the upper left panel the posterior view of the anatomic reconstruction of the left atrium and pulmonary veins obtained with an electroanatomic mapping system is shown. Pulmonary vein potentials (P) are recorded by a circular mapping catheter into the vein (arrows). Initial 2:1 conduction to the vein with subsequent complete block is observed (A: atrial potential).

**Table 1** Main randomized studies comparing antiarrhythmic drugs and ablation in paroxysmal AF. AAD: antiarrhythmic drugs. Parox: paroxysmal. AT: atrial tachycardia. AF: atrial fibrillation.

Study	Randomization	AF type	Age Ablation Group	N	Follow up	Number of procedures	Effectiveness (AADs vs ablation)
Packer <i>et al</i> <sup>[4]</sup> 2013 (STOP AF)	Ablation vs AADs	100% parox. resistant to $\geq 1$ AAD	56.7	245	9 months	$\geq 1$	7.3% vs 69.9% $p < 0.001$
Cosedis <i>et al</i> <sup>[16]</sup> 2012 (MANTRA-PAF)	Ablation first line	100% parox.	56 $\pm$ 9	294	24 months	1.6 $\pm$ 0.7	71% vs 85% $p = 0.004$
Morillo C <i>et al</i> <sup>[17]</sup> 2012 (RAAFT 2)	Ablation first line	87% parox.	55 $\pm$ 10 (bouth groups)	127	24 months		Time to first recurrence: 72% vs 54% $p = 0.01$
Wilber <i>et al</i> <sup>[5]</sup> 2010 (THERMOCOOL)	Ablation vs AADs	100% parox. resistant to $\geq 1$ AAD	55.5	167	9 months	1.8	16% vs 66% $p < 0.001$
Jais <i>et al</i> <sup>[6]</sup> 2008 (A4 study)	Ablation vs AADs	100% parox. resistant to $\geq 1$ AAD	49 $\pm$ 10	112	12 months	1.8	23% vs 89% $p < 0.001$
Papone <i>et al</i> <sup>[7]</sup> 2006 (APAF)	Ablation vs AADs	100% parox. resistant to $\geq 1$ AAD	55 $\pm$ 10	198	12 months	1	22% vs 86% $p < 0.001$
Stabile <i>et al</i> <sup>[8]</sup> 2006 (CACAF)	Ablation vs AADs	67% parox. resistant to $\geq 1$ AAD	62 $\pm$ 9	136	12 months	1	9% vs 56% $p < 0.001$
Wazni OM <i>et al</i> <sup>[15]</sup> 2005 (RAAFT)	Ablation first line	95% parox.	53 $\pm$ 8	70	12 months	1	37% vs 87% $p < 0.001$

therapy in the prevention of recurrences with follow-up periods between 9 and 12 months. These trials showed 56-89% success rates with ablative intervention versus 7-23% success rates in those treated with drug therapy (table 1)<sup>[4-8]</sup>.

Although with less evidence, we have data from randomized trials also showing greater efficacy in patients with persistent and long-lasting AF refractory to antiarrhythmic therapy<sup>[9,10]</sup>. The SARA study is the first multicenter, randomized study that compared antiarrhythmic therapy with catheter ablation in patients with persistent AF of less than one year, refractory to at least one class I or class III antiarrhythmic drug. After a follow-up period of 12 months, significantly fewer patients in the ablation group had recurrence of AF ablation or atrial flutter lasting more than 24 hours or need of cardioversion<sup>[9]</sup>.

Several meta-analysis have shown the superiority of ablation over antiarrhythmic therapy in the prevention of AF recurrences<sup>[11,12]</sup>. Data from randomized trials designed to address hard clinical outcomes such as stroke, heart failure or mortality are currently lacking and symptoms-control is nowadays the only well established rationale to perform AF ablation. However several registries have suggested a beneficial effect on the incidence of embolic events and mortality<sup>[13,14]</sup>. The currently ongoing CABANA trial has been designed to test the hypothesis that AF ablation is superior to drug therapy for decreasing the incidence of the composite endpoint of total mortality, disabling stroke, serious bleeding or cardiac arrest (ClinicalTrials.gov: NCT00911508).

Regarding AF ablation as first-line therapy, Wazni OM *et al* first published in 2005 a prospective multicenter randomized study of 70 patients comparing ablation vs antiarrhythmic therapy for symptomatic AF patients who had not received previous antiarrhythmic treatment. At one year follow-up, 63% of patients in the antiarrhythmic group compared to 13% undergoing ablation had an episode of AF ( $p < 0.01$ )<sup>[15]</sup>. New evidence in therapy-naive patients has been recently added<sup>[11,12]</sup>. In 2012 Cosedis NJ *et al* published a multicenter, randomized study comparing AF ablation as first-line therapy with antiarrhythmic therapy in 294 patients with a history of paroxysmal AF who were followed during 2 years. Follow-up included 7-days Holter monitor recording at 3,6,12,18 and 24 month. In patients randomized to ablation, circumferential pulmonary vein ablation was performed with a supplementary linear ablation placed along the roof of the left atrium between the two encircled areas. At the end of follow-up, the probability of remaining free of AF (85 vs 71 %,  $p = 0.004$ ) and symptomatic AF (93 vs 84 %,  $p = 0.01$ ) and quality of life were significantly higher in the ablation group. However, the cumulative burden of AF, which was the primary endpoint of the study, was not significantly different between the two treatment groups (13 % vs 19 %,  $p = 0.1$ )<sup>[16]</sup>. In the RAAFT 2 study, which included 127 patients with a history of paroxysmal or persistent AF not previously treated with AADs, a significant decrease in time to first AF in patients treated with pulmonary vein isolation was observed (54 vs 72 %,  $p = 0.01$ ). This trial still

awaits peer-reviewed publication<sup>[17]</sup>.

The results of these studies raised catheter ablation indication as first-line therapy in patients with symptomatic paroxysmal AF in the 2012 focused update of the European Society of Cardiology guidelines for the management of AF to a IIa indication (level of evidence B)<sup>[18]</sup> from a IIb indication (level of evidence B) in the previous european guideline published in 2010<sup>[19]</sup>. Previous to aforementioned works<sup>[16,17]</sup>, current guidelines on the management of patients with AF of the American Heart Association provides no indication of ablation as first-line treatment<sup>[20]</sup>.

European guidelines states that AF ablation as first-line treatment should be considered in selected patients with highly symptomatic paroxysmal AF provided it is performed in experienced centers and taking into account patient preference who must be adequately informed about the efficacy and safety of the different available treatment options<sup>[18]</sup>.

In addition to that stated in guidelines, other clinical characteristics can help us in the selection of these patients. In cases with frequent paroxysms of AF, we can offer higher success rates with a procedure aimed to the ablation of frequent activity atrial ectopic foci, in addition to electrical isolation of the pulmonary veins, especially if these foci were shown to trigger AF. The same happens when paroxysmal supraventricular tachycardia is suspected to cause AF. AF ablation is also the therapy of choice in order to maintain sinus rhythm in patients who present contraindications for antiarrhythmic therapy due to sinus bradycardia, conduction disturbances or channelopathies. Approximately 20% of patients with Brugada ECG pattern present AF. Yamada *et al*<sup>[21]</sup> described the utility of an AF ablation strategy without any antiarrhythmic drug in 6 patients with Brugada Syndrome and highly symptomatic AF. It should be consider that patients receiving ablation as first-line therapy must be well informed, motivated and not unwilling to undergo re-ablation procedures because data have shown a high incidence of recurrence in the medium term (4-5 years) after ablation and we know reablation improves efficacy<sup>[22]</sup>.

On the other hand AF ablation is still a complex intervention and probably highly dependent on the experience of the team performing the procedure. Real world data shows less favourable results than those published in randomized trials. The Atrial Fibrillation Ablation Pilot Study, conducted by the European Heart Rhythm Association, enrolled 1,410 patients undergoing AF ablation in 72 cardiology centres in 10 european countries. After one year follow up, 41% of patients were freedom from AF recurrence without AADs. The complication rate was 7%, with a major complication rate of 1.7%<sup>[23]</sup>.

AF ablation is currently a topic of intense research and some of them are providing encouraging results regarding the identification of the areas involved in AF maintenance in individual cases, opening the door to more targeted ablation strategies<sup>[24]</sup>. New technical developments have also emerged to facilitate procedures as cryoablation, laser ablation, circular ablation catheters and evolved electroanatomic

mapping systems. The key to be able to offer catheter ablation to an increasing number of patients is to achieve an adequate combination of good clinical results and low complication rates. Although much effort remains to be done, we believe that technical evolution and the increasing expertise of teams performing ablation are allowing us to treat our patients with safer and more effective procedures. That is why AF ablation as first-line therapy is here to stay and probably we will be witness of a further extension of the indications, for instance to selected asymptomatic patients, as already happened in other arrhythmic substrates.

## CONFLICT OF INTERESTS

There are no conflicts of interest with regard to the present study.

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