

# Does catheter ablation cure atrial fibrillation? Single-procedure outcome of drug-refractory atrial fibrillation ablation: a 6-year multicentre experience

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## Aims

In the last decade, several approaches to ablating triggers and substrates of atrial fibrillation (AF) have been developed. However, most studies have reported data only on short- or medium-term follow-up. The aim of this study was to investigate whether the 1-year efficacy of catheter ablation for AF is predictive of long-term clinical success.

## Methods and results

Between February 2001 and October 2003, 229 consecutive patients affected by drug-refractory paroxysmal or persistent AF underwent a single radiofrequency catheter ablation procedure (anatomical approach in 146 patients and electrophysiologically guided approach in 83 patients). Of these patients, 177 (mean age  $59.1 \pm 10.5$  years, 57.6% with paroxysmal AF) were free from any atrial arrhythmia recurrence after 12 months. These 177 patients were subsequently followed up for at least another 24 months, by means of electrocardiogram and 24 h Holter monitoring. After a mean follow-up of  $49.7 \pm 13.3$  months (range 36–83 months), 58.2% of the patients were free from any atrial arrhythmia recurrence (39.5% without antiarrhythmic drugs). The actuarial atrial arrhythmia recurrence rate was 13.0% at 2 years, 21.8% at 3 years, 35.0% at 4 years, 46.8% at 5 years, and 54.6% at 6 years. Atrial arrhythmia-free survival was similar in patients with paroxysmal or persistent AF, with and without antiarrhythmic drugs during the follow-up, who underwent electrophysiologically guided pulmonary vein (PV) isolation or anatomical PV ablation.

## Conclusion

Even patients in whom catheter ablation prevents AF recurrence for 1 year should not be considered 'cured', since >40% of them will suffer AF recurrence over a long-term clinical follow-up.

## Keywords

Atrial fibrillation • Catheter ablation • Long-term results

## Introduction

The discovery of the role of the pulmonary veins (PVs) in initiating and perpetuating atrial fibrillation (AF) has led to the ablative treatment of AF.<sup>1–2</sup> In the last decade, several approaches<sup>3–6</sup> to ablating triggers and substrates of AF have been developed, all of which have proved able to prevent AF recurrence in up to 80–90% of

patients. However, most studies have reported data only on short- or medium-term follow-up, usually no longer than 12 months. Atrial fibrillation is linked to age-related physiological modifications of atrial anatomy. Thus, unlike arrhythmias related to inherited substrates, such as Kent fibres or dual atrioventricular pathway, in which short-term success correlates very well with long-term outcome, in the case of AF, this correlation may not

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be true. The aim of this retrospective study was to evaluate whether in patients with drug-refractory AF in whom catheter ablation had prevented arrhythmia recurrence during the first year of follow-up, the efficacy of catheter ablation persisted over long-term follow-up.

## Methods

### Patient characteristics and study design

Between February 2001 and October 2003, 229 consecutive patients affected by drug-refractory paroxysmal or persistent AF underwent radiofrequency (RF) catheter ablation (electro-anatomical approach in 146 patients and electrophysiologically guided approach in 83 patients) in three Italian centres. Paroxysmal AF was defined as self-terminating AF episodes lasting <7 days. Persistent AF was defined as AF episodes lasting  $\geq 7$  days or requiring pharmacological or electrical cardioversion because of intolerable symptoms.<sup>7</sup> Patients with permanent AF, i.e. AF as the sole rhythm for the last 6 months, were not included in this study. Of these 229 patients, 177 (78%) remained free from any atrial arrhythmia recurrence, both AF and atrial flutter, during a 12-month follow-up after a single ablation. This group was further followed up for at least 24 months, and the incidence of atrial arrhythmia recurrence was evaluated. This observational study was approved by each institutional review committee, and all patients provided written informed consent for the ablation procedure.

### Electrophysiological study and catheter ablation

Prior to electrophysiological study, transoesophageal echocardiography was performed in order to exclude left atrial (LA) thrombus. All patients received effective oral anticoagulation (international normalized ratio between 2 and 3) for  $\geq 1$  month before ablation. Heparin anticoagulation replaced oral anticoagulants  $\geq 72$  h before ablation and was discontinued 4 h before the procedure. Patients were studied in a conscious state, a bolus of pethidine hydrochloride, midazolam, or propofol being administered in the event of intolerable pain during ablation. A quadripolar or decapolar catheter was inserted through the femoral, jugular, subclavian, or antecubital vein into the coronary sinus. In all patients, the LA and PVs were explored by means of a trans-septal approach. After trans-septal puncture, an intravenous bolus of heparin (5000 IU) was administered, followed by infusion or additional boluses to maintain an activated clotting time  $\geq 250$  s.

In patients who underwent the electro-anatomical approach, real-time 3D LA maps were reconstructed by using a non-fluoroscopic navigation system (CARTO™, Biosense Webster Inc., Diamond Bar, CA, USA). Maps were acquired during AF or pacing from the coronary sinus, as described previously.<sup>8</sup> Radiofrequency pulses were delivered by using the mapping catheter (Navistar™, Biosense Webster Inc.) (8 mm tip with a temperature setting of 60°C and RF energy up to 70 W, or 3.5 mm irrigated-tip catheter with a temperature setting up to 45°C, RF energy up to 40 W, and an irrigation rate up to 30 mL/min). Radiofrequency energy was delivered for up to 120 s until local electrogram amplitude was reduced by  $\geq 80\%$ . The ablation lines consisted of contiguous focal lesions deployed at a distance of  $\geq 5$  mm from the ostia of the PVs in order to create a circumferential line around each PV. Another ablation line was created by connecting the left inferior PV to the mitral annulus (mitral isthmus). The endpoint of the PV ablation was low peak-to-peak bipolar potentials (<0.1 mV)

inside the lesion, as revealed by local electrogram analysis and voltage maps. A minimum of five points for each circumferential line were sampled. If sites of high voltage (>0.1 mV) were still present, additional ablations were performed, both along and within the encircling ablation lines. The endpoint of mitral isthmus line ablation was evaluated by pacing from the distal electrodes of the coronary sinus catheter and recording on the distal electrodes of the ablation catheter, positioned on that line, a double potential with an isoelectric line of at least 80 ms.

In patients who underwent the electrophysiological approach, two catheters were inserted into the LA: a multipolar steerable circular catheter for circumferential PV mapping (LASSO™, Biosense Webster Inc.), and an 8 mm tip catheter (Celsius dual temperature, Biosense Webster Inc.) or an irrigated 3.5 mm tip catheter (Thermo-Cool™, Biosense Webster, Inc.) for ablation. After entering the PV, the circular catheter was positioned as close as possible to the PV ostium. Pulmonary vein isolation was obtained by delivering RF energy to those ostial sites which showed electrical breakthroughs.<sup>3</sup> Radiofrequency was applied in a temperature-control mode with a temperature setting up to 60°C and RF energy up to 70 W while using an 8 mm tip ablation catheter, and in a power-control mode with RF energy up to 35 W while using an irrigated-tip catheter. The endpoint of the ablation procedure was PV isolation, as documented by the disappearance or disconnection of PV potentials. Cavotricuspid isthmus ablation was performed at the end of LA ablation in all patients, apart from those in whom it had been performed during a previous procedure. Patients who were still in AF at the end of ablation underwent electrical cardioversion before cavotricuspid isthmus ablation.

### Post-ablation management

All patients were discharged on oral anticoagulants and continued their antiarrhythmic drugs for at least 3 months. Transoesophageal and transthoracic echocardiography was performed after 3 months to assess PV stenosis, mitral valve function, and left ventricular ejection fraction. Clinical examination, electrocardiogram (ECG), and 24 h Holter monitoring were performed after 3, 6, and 12 months. Patients in stable sinus rhythm after the first 6 months were encouraged to discontinue antiarrhythmic drugs. Patients who maintained sinus rhythm, with or without antiarrhythmic drugs, for the 12-month follow-up period constituted the study group. These patients continued to be monitored every 6 months by means of outpatient clinical examinations, ECG, and 24 h Holter monitoring for at least another 24 months. The primary endpoint of the study was experience/detection of any atrial arrhythmias lasting >30 s, on or off antiarrhythmic drugs, after a single ablation procedure.

### Statistical analysis

Continuous measurements were expressed as mean  $\pm$  SD and were compared by means of Student's *t*-test. The normality of distribution of continuous variables was assessed by visual inspection of the histograms. Discrete variables were analysed by  $\chi^2$  or Fisher's exact test; relative risk and 95% confidence interval were calculated. Single-variable Cox's regression analysis was used for the search of predictors of sinus rhythm maintenance. Variables with  $P < 0.3$  on univariate analysis were fitted into a multivariate non-linear regression model. A Kaplan–Meier analysis with the log-rank test was used to determine the probability of freedom from AF recurrence. All tests were two-tailed. A *P*-value <0.05 was considered statistically significant. Analysis was performed by means of the Statistical Package for the Social Sciences (SPSS, version 11.0) (SPSS, Inc., Chicago, IL, USA).

## Results

### Clinical and procedural characteristics

Clinical characteristics of the 177 study patients are shown in Table 1. Of note, most suffered from paroxysmal AF and had a long arrhythmic history. Although 42.9% presented a structural heart disease—hypertensive cardiopathy in most cases—the left ventricular ejection fraction was within the normal limit, and the left atrium only mildly dilated.

Most of our patients (110/177, 62.1%) underwent electro-anatomical ablation, whereas electrophysiologically guided ablation was performed in 67/177 (37.9%). Inferior vena cavitricuspid annulus isthmus ablation was performed, in the same session, in 61/177 patients (34.5%).

### Clinical outcome

Patients were followed up for a mean of  $49.7 \pm 13.3$  months (range 36–83 months). Five deaths (2.8%) occurred: two non-cardiovascular deaths and three cardiovascular deaths, all sudden. During follow-up, AF recurred in 74/177 patients (41.8%). We did not observe atrial tachyarrhythmias other than AF. Paroxysmal AF was the most frequent type of recurrent AF (38 patients, 21.5%), followed by permanent AF (20 patients, 11.3%), and persistent AF (16 patients, 9.0%). The evolution of AF in patients with recurrences is presented in Figure 1.

The actuarial atrial arrhythmia recurrence rate was 13.0% at 2 years, 21.8% at 3 years, 35.0% at 4 years, 46.8% at 5 years, and 54.6% at 6 years (Figure 2).

In 33 patients (18.6%), sinus rhythm was maintained on anti-arrhythmic drugs (amiodarone in 16 patients, flecainide in 8, propafenone in 5, and sotalol in 4). The actuarial curves of freedom from AF, with and without antiarrhythmic drugs, are presented in Figure 3. The cumulative probability of maintaining sinus rhythm did not prove significantly different between these two groups of patients.

**Table 1 Clinical characteristics**

|                            | <i>n</i> = 177  |
|----------------------------|-----------------|
| Male (%)                   | 74.6            |
| Age (years)                | $59.1 \pm 10.5$ |
| Paroxysmal AF (%)          | 57.6            |
| AF duration (years)        | $5.3 \pm 3.8$   |
| SHD (%)                    | 42.9            |
| Hypertensive HD (%)        | 31.7            |
| Dilated cardiomyopathy (%) | 5.5             |
| Ischemic HD (%)            | 3.5             |
| Valvular HD (%)            | 2.2             |
| Left atrial size (mm)      | $46.1 \pm 4.3$  |
| LVEF (%)                   | $57.7 \pm 6.6$  |

AF, atrial fibrillation; LVEF, left ventricular ejection fraction; SHD, structural heart disease.

### Predictors of atrial fibrillation-free survival

Of several clinical and procedural variables considered, none proved to be correlated with long-term maintenance of sinus rhythm (Table 2) at both univariate and multivariate analysis. We observed only a trend towards a better result in patients with a small LA. Specifically, the cumulative probability of sinus rhythm maintenance was not significantly different between patients with paroxysmal AF and those with persistent AF (Figure 4), nor between patients who underwent electrophysiologically guided PV isolation and those who underwent anatomical PV ablation (Figure 5).

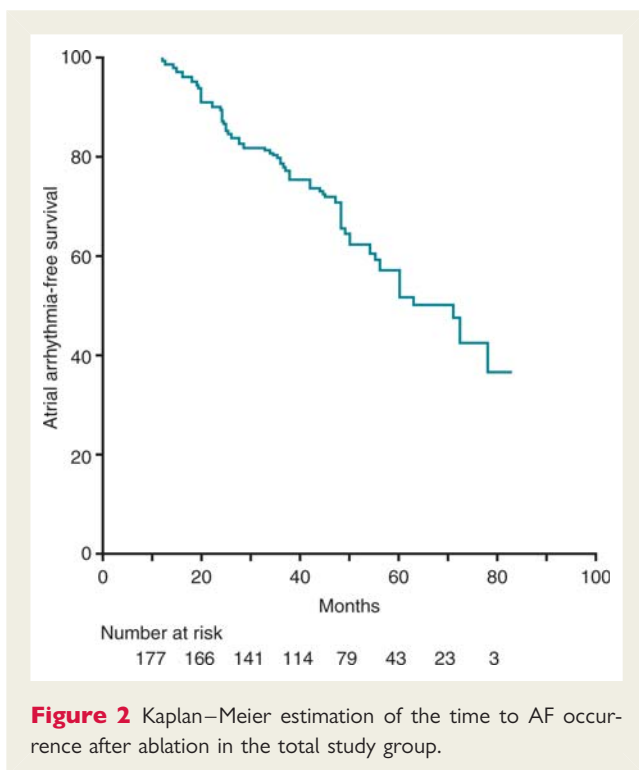
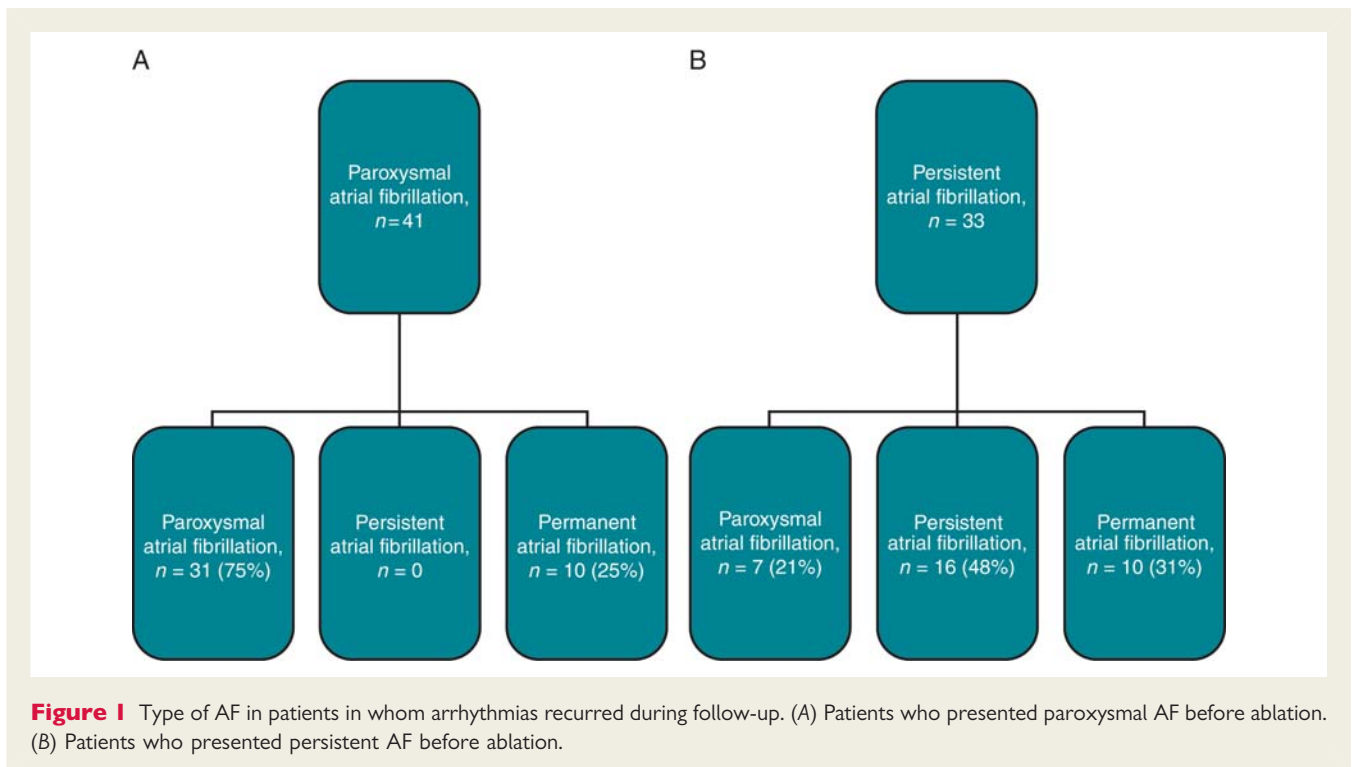
## Discussion

### Main findings

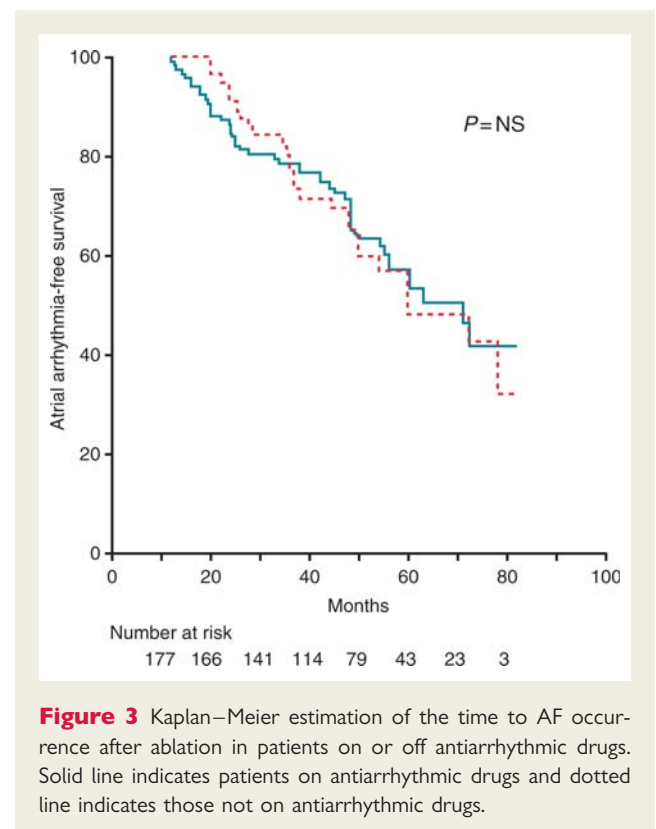
This observational retrospective study evaluated the long-term outcome of a large multicentre series of consecutive patients with drug-refractory AF who underwent a single catheter ablation procedure. Approximately 40% of the patients who were free from any arrhythmia recurrence 1 year after ablation suffered AF recurrence during the next 3 years. The efficacy of electrophysiologically guided PV isolation and anatomical PV ablation proved to be similar. Atrial fibrillation-free survival was similar in patients with paroxysmal AF and in those with persistent AF, and in patients on or off antiarrhythmic drugs.

### Long-term efficacy of atrial fibrillation ablation

Although catheter ablation of AF has emerged as an important treatment option for patients with symptomatic AF,<sup>9–11</sup> its long-term safety and efficacy are still unknown.<sup>12–13</sup> The large number of anatomical and electrophysiological substrates that initiate and/or maintain AF,<sup>14</sup> and their physiological modification with ageing, makes it unlikely that short-term success will correlate with long-term outcome. So far, few studies have investigated what happens after the first 12 months following AF ablation,<sup>15–22</sup> and only three have involved a mean follow-up longer than 3 years.<sup>19,21,22</sup> Katritsis *et al.*<sup>19</sup> followed up 39 patients suffering from paroxysmal AF for  $42.2 \pm 6.0$  months after segmental PV isolation. Fiala *et al.*<sup>21</sup> reported the results of a randomized study on paroxysmal AF ablation in which they compared two different techniques (segmental PV isolation and circumferential PV isolation) in 110 patients, who were followed up for a mean of  $48 \pm 8$  months after ablation. What is striking is the different clinical outcome observed in these two studies, even though the populations studied were similar and the follow-up duration was the same. In the study of Katritsis *et al.*, long-term success without antiarrhythmic drugs after a single ablation procedure was very poor (8%), whereas Fiala *et al.* reported that 56% of the patients were free from arrhythmia after the first ablation, without antiarrhythmic drugs. This significant discrepancy cannot be explained in terms of ablation technique, as in Fiala *et al.*'s study, the long-term success rate was similar for the two techniques: segmental PV isolation and circumferential PV isolation. Intermediate data



were reported by Gaita et al.<sup>22</sup> In their study, 204 consecutive patients symptomatic for paroxysmal or persistent/permanent AF were randomly assigned to two different ablation schemes: PV isolation or PV isolation plus left linear lesions. Among patients with paroxysmal AF who had undergone a single procedure, 29% of those treated with PV isolation and 53% of those treated with

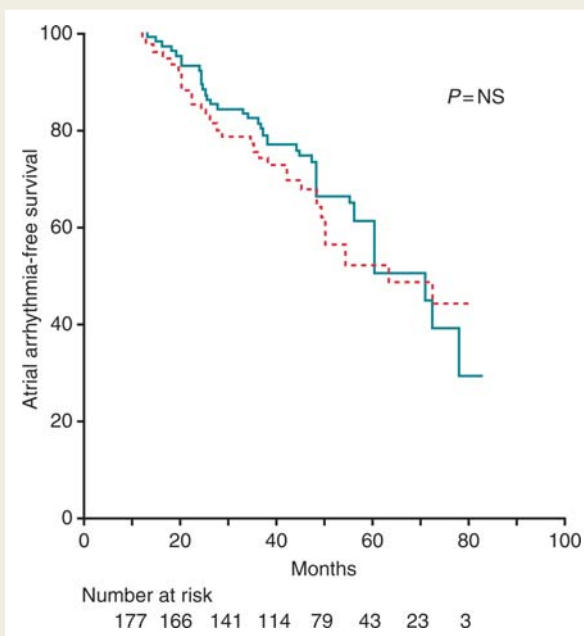


PV isolation plus left linear lesions maintained sinus rhythm over a 3-year follow-up. Among patients with persistent/permanent AF, only 19% of those treated with PV isolation maintained sinus rhythm over the 3-year follow-up, whereas 41% of the patients

**Table 2 Predictors of sinus rhythm maintenance: univariate analysis**

|                                 | Atrial fibrillation (n = 74) | Sinus rhythm (n = 103) | P-value |
|---------------------------------|------------------------------|------------------------|---------|
| Age (years)                     | 58.5 ± 10.6                  | 59.5 ± 10.5            | 0.52    |
| Male gender (%)                 | 62.2                         | 56.8                   | 0.53    |
| SHD (%)                         | 61.4                         | 53.9                   | 0.32    |
| Paroxysmal AF (%)               | 56.0                         | 59.8                   | 0.61    |
| Left atrial size (mm)           | 46.7 ± 4.4                   | 45.6 ± 4.2             | 0.08    |
| LVEF (%)                        | 57.2 ± 6.5                   | 58.0 ± 6.8             | 0.47    |
| Electro-anatomical ablation (%) | 65.7                         | 53.6                   | 0.12    |
| Right isthmus ablation (%)      | 62.1                         | 50.8                   | 0.15    |

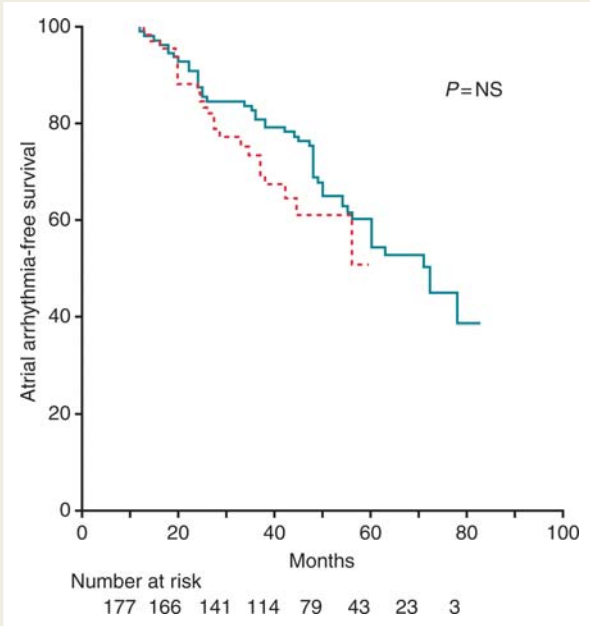
AF, atrial fibrillation; LVEF, left ventricular ejection fraction; SHD, structural heart disease.



**Figure 4** Kaplan–Meier estimation of the time to AF occurrence after ablation in patients with paroxysmal or persistent AF. Solid line indicates patients with paroxysmal AF and dotted line indicates those with persistent AF.

treated with PV isolation plus left linear lesions achieved this result.<sup>22</sup>

In our study, 58.2% of the patients were free from arrhythmia after 4 years (45% of the original 229 patients), 18.6% of whom continued antiarrhythmic therapy. These results seem to confirm those of Fiala *et al.*<sup>21</sup> and Gaita *et al.*<sup>22</sup> What is new in our data is that for the first time, no difference in the AF recurrence rate emerged between paroxysmal and persistent AF patients over a very long time after a single ablation procedure. Although the



**Figure 5** Kaplan–Meier estimation of the time to AF occurrence after ablation in patients who underwent anatomical pulmonary vein ablation or electrophysiologically guided pulmonary vein isolation. Solid line indicates anatomical pulmonary vein ablation and dotted line indicates electrophysiologically guided pulmonary vein isolation.

efficacy of PV ablation in persistent AF patients is less predictable, a better long-term outcome of PV isolation may be expected in paroxysmal AF patients, in whom the role of triggers is apparently predominant. Our findings, however, seem not to support this hypothesis. Of note, during a mean follow-up of ~4 years, 11.2% of our patients who underwent ablation for persistent or paroxysmal AF evolved to permanent AF. A similar rate of progression to permanent AF was reported in the Olmsted County study by Jahangir *et al.*<sup>23</sup> In their study, in a cohort of 71 patients with lone paroxysmal (*n* = 34) or persistent AF (*n* = 37) treated with antiarrhythmic drugs, 7 patients (9.9%) suffered progression to permanent AF within 5 years. Comparison of the results of the two studies suggests that a single procedure of catheter ablation is unable to prevent progression to permanent AF. Organized atrial arrhythmias are reported to occur in 3–10% of the patients after PV ablation.<sup>24–26</sup> In contrast to these findings, we did not observe any organized atrial arrhythmias after the first 12 post-ablation months. However, all previous reports regarding post-ablation atrial flutter or tachycardias refer to short-term follow-up. On increasing the duration of follow-up, the rate of these arrhythmias seems to decrease.<sup>19,21,22</sup>

### Predictors of long-term sinus rhythm maintenance

Our findings did not allow us to identify any predictors of very long-term sinus rhythm maintenance. We only observed that patients with an enlarged LA had a lower probability of maintaining sinus rhythm; this could be confirmed by increasing the number of



study patients. No other study has investigated this issue in the setting of very late recurrences, although Shah *et al.*<sup>20</sup> found that hypertension and hyperlipaemia characterized patients with late recurrences among 264 patients followed up for a shorter period ( $28 \pm 12$  months).

## Study limitations

An important limitation is that this was an observational study. Nevertheless, observational studies like this can provide additional information, since they are fully representative of actual clinical practice, in which several factors that are underestimated in prospective trials, such as the different experience of the centres involved, may play a role. For this reason, observational studies will be of particular importance in monitoring and guiding the incorporation of this therapeutic procedure into clinical practice.

The cumulative probability of sinus rhythm maintenance did not prove significantly different between patients who underwent electrophysiologically guided PV isolation and those who underwent anatomical PV ablation. However, the fact that our experience with electrophysiologically guided PV isolation was shorter than that with anatomical PV ablation might have affected this result.

To assess the block along the mitral isthmus, we used only the presence of widely separated local double potentials along the length of the ablation line during coronary sinus pacing, and not also the mapping of the activation detour during pacing from either side of the line and the differential pacing to distinguish slow conduction across the isthmus from complete block, as described by Jais *et al.*<sup>27</sup> Our technique might have overestimate the percentage of patients in which the bidirectional block was really achieved thus increasing the probability of LA flutter recurrences after ablation. However, this limitation should have not influenced our long-term results since we decided to evaluate the outcome only of patients free of any arrhythmia, both AF and atrial flutter, after 1-year of follow-up.

Another potential limitation is that 33 of our patients (18.6%) who remained in sinus rhythm were on antiarrhythmic drugs. However, the cumulative probability of sinus rhythm maintenance did not prove significantly different between patients on antiarrhythmic drugs and those not on such drugs. Similar data have recently been reported by Turco *et al.*,<sup>28</sup> who observed that continuing antiarrhythmic drug therapy did not lower AF recurrences after catheter ablation for AF, whereas antiarrhythmic drugs increased the proportion of patients with asymptomatic AF episodes.

## Conclusions

Data from published studies and from our experience seem to confirm that success over a 12-month follow-up does not necessarily guarantee permanent success, and that the early hope of AF ablation being a 'curative' procedure continues to be shattered by the harsh reality that AF does in fact recur after a several-month blanking period.<sup>29</sup> Thus, AF ablation seems to have a 'palliative' rather than 'curative' effect, at least in most patients. This fact raises concerns about the risk of discontinuing anticoagulation after short-term success in patients with risk factors for thrombo-embolic events. Multiple ablation procedures might increase the long-term rate of patients free from AF.<sup>22</sup>

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## References

- Jais P, Haïssaguerre M, Shah DC, Chouairi S, Gencel L, Hocini M *et al.* A focal source of atrial fibrillation treated by discrete radiofrequency ablation. *Circulation* 1997;**95**:572–6.
- Haïssaguerre 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.
- Haïssaguerre M, Shah DC, Jais P, Hocini M, Yamane T, Deisenhofer I *et al.* Electrophysiological breakthroughs from the left atrium to the pulmonary veins. *Circulation* 2000;**102**:2463–5.
- Pappone C, Rosanio S, Oreto G, Tocchi M, Gugliotta F, Vicedomini G *et al.* Circumferential radiofrequency ablation of pulmonary vein ostia. *Circulation* 2000;**102**:2619–28.
- Marrouche NF, Martin DO, Wazni O, Gillinov AM, Klein A, Bhargava M *et al.* Phased-array intracardiac echocardiography monitoring during pulmonary vein isolation in patients with atrial fibrillation: impact on outcome and complications. *Circulation* 2003;**107**:2710–6.
- Nademanee K, McKenzie J, Kosar E, Schwab M, Sunsaneewitayakul B, Vasavakul T *et al.* A new approach for catheter ablation of atrial fibrillation: mapping of the electrophysiologic substrate. *J Am Coll Cardiol* 2004;**43**:2044–53.
- Levy S, Camm J, Saksena S, Aliot E, Breithard G, Crijns HJGM *et al.* International consensus on nomenclature and classification of atrial fibrillation: a collaborative project of the working group on arrhythmias and the working group of cardiac pacing of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. *J Cardiovasc Electrophysiol* 2003;**14**:443–5.
- Bertaglia E, Stabile G, Senatore G, Colella A, Del Greco M, Goessinger H *et al.* A clinical and health-economic evaluation of pulmonary vein encircling ablation compared with antiarrhythmic drug treatment in patients with persistent atrial fibrillation (Catheter Ablation for the Cure of Atrial Fibrillation-2 Study). *Europace* 2007;**9**:182–5.
- Wazni OM, Marrouche NF, Martin DO, Verma A, Bhargava M, Saliba W *et al.* Radiofrequency ablation vs antiarrhythmic drugs as first-line treatment of symptomatic atrial fibrillation: a randomized trial. *JAMA* 2005;**293**:2634–40.
- Stabile G, Bertaglia E, Senatore G, De Simone A, Zoppo F, Donnici G *et al.* Catheter ablation treatment in patients with drug-refractory atrial fibrillation: a prospective, multi-centre, randomized, controlled study (Catheter Ablation For The Cure Of Atrial Fibrillation Study). *Eur Heart J* 2006;**27**:216–21.
- Oral H, Pappone C, Chugh A, Good E, Bogun F, Pelosi F Jr *et al.* Circumferential pulmonary vein ablation for chronic atrial fibrillation. *N Engl J Med* 2006;**354**:934–94.
- Natale A, Raviele A, Arents T, Calkins H, Chen SA, Haïssaguerre M *et al.* Venice Chart International Consensus Document on Atrial Fibrillation Ablation. *J Cardiovasc Electrophysiol* 2007;**18**:560–80.
- Calkins H, Brugada J, Packer D, Cappato R, Chen SA, Crijns HJ *et al.* HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for personnel, policy, procedures and follow-up. *Heart Rhythm* 2007;**4**:816–61.
- Fuster V, Rydén LE, Cannom DS, Crijns HJ, Curtis AB, Ellenbogen KA *et al.* ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 Guidelines for the Management of Patients With Atrial Fibrillation). *J Am Coll Cardiol* 2006;**48**:e149–e246.
- Bertaglia E, Stabile G, Senatore G, Turco P, Donnici G, De Simone A *et al.* Long term outcome of right and left atrial radiofrequency ablation in patients with persistent atrial fibrillation. *Pacing Clin Electrophysiol* 2006;**29**:153–8.
- Solheim E, Hoff PI, Off MK, Ohm OJ, Chen J. Significance of late recurrence of atrial fibrillation during long-term follow-up after pulmonary vein isolation. *Pacing Clin Electrophysiol* 2007;**30**:S108–11.
- Sartini RP, Scanavacca MI, Sosa E, Moreira LF, Lara S, Hardy C *et al.* Radiofrequency ablation of paroxysmal atrial fibrillation: factors determining long term clinical efficacy. *Arq Bras Cardiol* 2008;**90**:112–8.
- Cheema A, Vasamreddy CR, Dalal D, Marine JE, Dong J, Henrikson CA *et al.* Long-term single procedure efficacy of catheter ablation of atrial fibrillation. *J Interv Card Electrophysiol* 2006;**15**:145–55.
- Katritsis D, Wood MA, Giazitzoglou E, Shepard RK, Kourlaba G, Ellenbogen KA. Long-term follow-up after radiofrequency catheter ablation for atrial fibrillation. *Europace* 2008;**10**:419–24.

20. Shah AN, Mittal S, Sichrovsky TC, Cotiga D, Arshad A, Maleki K *et al*. Long-term outcome following successful pulmonary vein isolation: pattern and prediction of very late recurrence. *J Cardiovasc Electrophysiol* 2008;**19**:661–7.
21. Fiala M, Chovancik J, Nevalova R, Neuwirth R, Jiravsky O, Nykl I *et al*. Pulmonary vein isolation using segmental versus electroanatomical circumferential ablation for paroxysmal atrial fibrillation. Over 3-year results of a prospective randomized study. *J Interv Card Electrophysiol* 2008;**22**:13–21.
22. Gaita F, Caponi D, Scaglione M, Montefusco A, Corleto A, Di Monte F *et al*. Long-term clinical results of 2 different ablation strategies in patients with paroxysmal and persistent atrial fibrillation. *Circ Arrhythmia Electrophysiol* 2008;**1**:269–75.
23. Jahangir A, Lee V, Friedman PA, Trusty JM, Hodge DO, Kopecky SL *et al*. Long-term progression and outcomes with aging in patients with lone atrial fibrillation. A 30-year follow-up study. *Circulation* 2007;**115**:3050–6.
24. Cummings JE, Schweikert R, Saliba W, Hao S, Martin DO, Marrouche NF *et al*. Left atrial flutter following pulmonary vein antrum isolation with radiofrequency energy: linear lesions or repeated isolation. *J Cardiovasc Electrophysiol* 2005;**16**:298–301.
25. Gerstenfeld EP, Callans DJ, Sauer W, Jacobson J, Marchlinski FE. Reentrant and nonreentrant focal left atrial tachycardias occur after pulmonary vein isolation. *Heart Rhythm* 2005;**2**:1195–202.
26. Chae S, Oral H, Good E, Dey S, Wimmer A, Crawford T *et al*. Atrial tachycardia after circumferential pulmonary vein ablation of atrial fibrillation. *J Am Coll Cardiol* 2007;**50**:1781–7.
27. Jais P, Hocini M, Hsu LF, Sanders P, Scavee C, Weerasooriya R *et al*. Technique and results of linear ablation at the mitral isthmus. *Circulation* 2004;**110**:2996–3002.
28. Turco P, De Simone A, La Rocca V, Iuliano A, Capitano V, Astarita C *et al*. Anti-arrhythmic drug therapy after radiofrequency catheter ablation in patients with atrial fibrillation. *Pacing Clin Electrophysiol* 2007;**30**:S112–S115.
29. Calkins H. Further insight into the technique and outcomes of 'curative' catheter ablation of atrial fibrillation. *Circ Arrhythmia Electrophysiol* 2008;**1**:238–9.