Long-term follow-up after radiofrequency catheter ablation of atrial fibrillation: Role of the acute procedure outcome and of the clinical presentation

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Submitted 25 May 2004, and accepted after revision 12 December 2004

Abstract Aims This study is a single centre long-term experience on a consecutive cohort of patients with paroxysmal or persistent atrial fibrillation (AF) undergoing electrical disconnection of pulmonary veins (PVs) by means of catheter ablation. Long-term outcome was analyzed in relation to acute procedure success and to the clinical presentation.

Methods and results Two hundred and thirty-four patients (182 males, mean age 55.9 ± 10.6 years), affected by paroxysmal (78%) or persistent AF, underwent an electrophysiologically guided isolation of PVs. ECG, Holter and clinical follow-up were obtained at 1, 3, 6 and 12 months. At discharge an antiarrhythmic drug, Flecainide, was given only in cases with incomplete disconnection; Amiodarone was administered in all persistent AF pts.

Successful disconnection of all PVs was achieved in 90% of cases. The rate of stable sinus rhythm maintenance was 85%, 74%, 72% and 65% at 1, 3, 6 and 12 months, respectively. The one-year arrhythmia free survival rates were higher among patients with paroxysmal AF (68% vs. 54%, P = 0.008), those with complete disconnection of all PVs and in patients younger than 55 years.

Conclusions The electrical disconnection of all the pulmonary veins should be the minimal endpoint of radiofrequency catheter ablation in patients with either paroxysmal or persistent AF. Incomplete disconnection of the PVs is predictive of
recurrence. Long-term results of the ablation procedure were significantly better in patients with paroxysmal AF.

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Introduction

Electrical disconnection of the pulmonary veins from the left atrium by radiofrequency catheter ablation is currently the most frequently undertaken approach when non-pharmacological treatment of atrial fibrillation is considered. The rationale of the procedure relies on the seminal observations by Haïssaguerre et al., providing evidence that atrial fibrillation is most frequently triggered by ectopic foci located within the pulmonary veins or at the junction of the veins and the left atrium [1]. Initial attempts at mapping and eliminating triggers within the pulmonary veins, although acutely effective, resulted in high recurrence rates; furthermore, only a minority of patients qualified for the procedure due to insufficient ambient ectopy [1,2]. The introduction of circumferential mapping catheters that can be sequentially advanced to the ostium of all pulmonary veins has provided a significant improvement in the study of the pattern of bidirectional conduction [3–6]. Furthermore, it allows the assessment of a standard endpoint of the procedure (conduction block to and from the pulmonary veins), which can be obtained during stable sinus rhythm. A substantial long-term beneficial effect following this procedure has been reported in several series [5,7], ranging from complete eradication of the arrhythmia to improved arrhythmia control by previously ineffective antiarrhythmic drugs.

Less information is however available concerning the timing of arrhythmia recurrence, the need for repeated ablation procedures and/or continued antiarrhythmic and anticoagulant drug treatment following isolation of the pulmonary veins. In this manuscript, a single centre long-term experience is reported on a consecutive cohort of patients undergoing the same treatment protocol for the treatment of atrial fibrillation. In particular, the rate of long-term control of arrhythmia recurrence following catheter ablation was analysed in relation to acute procedure outcome (achievement of complete electrical disconnection of all the pulmonary veins from the left atrium) and to the clinical presentation of the arrhythmia (paroxysmal vs. persistent) [8]. The role of in-hospital rhythm monitoring following the procedure to guide the decision of whether to perform an additional procedure and/or the need for prolonged antiarrhythmic treatment is also described and analysed in comparison with the subsequent outcome [9].

Methods

Patient characteristics

Two hundred and thirty-four consecutive patients (182 males, mean aged 55.9 ± 10.6 years; rate 22–78) underwent a catheter ablation procedure for atrial fibrillation at our Institution between March 2001 and September 2003. The arrhythmia was paroxysmal in 183 (78%) and persistent in 51 (22%) patients. Patients with paroxysmal AF were symptomatic for a mean of 6.2 ± 5.3 years and had failed pharmacological treatment with at least two drugs (amiodarone + 1c antiarrhythmic drug). Amiodarone was not tried in patients less than 50 years old. AF was considered persistent when it was present for more than 60 days despite repeated attempts at pharmacological cardioversion and when external DC shock was required to restore sinus rhythm. Most patients were free from structural heart disease; the clinical characteristics of the study population are shown in Table 1.

Electrophysiological procedure

Treatment with antiarrhythmic drugs was discontinued in all patients three days before the procedure; amiodarone was withdrawn at least 6 weeks before hospitalisation. All patients with persistent AF underwent a transoesophageal echocardiogram to rule out the presence of thrombi in the left atrium or left atrial appendage. Oral anticoagulation was replaced by IV heparin anticoagulation for at least 24 h. At the beginning of the ablation, sinus rhythm was restored by external cardioversion [10]. All patients had provided written informed consent. At the electrophysiological study, a decapolar electrode catheter (Daig CSL, Minnetonka, MN, USA) was advanced to the coronary sinus from the right internal jugular vein. Access to the left atrium was achieved through a patent foramen ovale (11/234 pts, 4.7%) or by transseptal puncture (Preface Multipurpose, Biosense Webster); the transseptal sheath was...
continuously rinsed with heparinized saline and withdrawn to the right atrium whenever possible during the procedure. Systemic anticoagulation was obtained by intravenous heparin to maintain an activated clotting time of 200–300 s. Selective angiograms of the PVs were obtained in the 45° left and right anterior oblique projections. Mapping of the PV ostia was performed with a decapolar circumferential catheter, (Lasso catheter, Biosense Webster, Diamond Bar, California): a second catheter was used for single point mapping and ablation. At the beginning, the choice of an irrigated-tip catheter was limited to selected cases where target power could not be obtained because of low local blood flow; since September 2002 an irrigated-tip catheter was used as first choice according to the evidence of feasibility and safety of this approach [11]. Pulmonary vein muscle potentials were recorded in bipolar mode from 10 bipoles (1–2, 2–3, etc.). Bipolar electrograms were filtered at band pass settings of 30–500 Hz, respectively, and were recorded digitally (Prucka Systems, GE). Pacing was performed from the distal coronary sinus with a programmable stimulator (Bloom Electrophysiology, Denver Colorado, USA). RF energy was delivered at the distal electrode of the thermocouple-equipped catheter (target: 50 °C) with a power limit of 25–30 W; pulse duration ranged from 120 to 600 s. The irrigated-tip catheter (17 ml/min saline flow) was used with a target temperature of 43 °C and the same power settings. RF ablation was performed at the ostium of each vein, pointing to the bipole of the circular catheter where atrial and PV electrograms were fused showing the earliest activation during pacing of the distal coronary sinus for the left veins, pacing from the proximal coronary sinus for the right inferior vein or during sinus rhythm for the right superior vein. The end point was elimination of PV muscle conduction distal to the ablation site for all veins (Figs. 1 and 2). In the instances when the circumferential mapping catheter could not be positioned at the right inferior vein ostium, RF ablation was performed around its ostium and the endpoint of PV isolation then assessed by mapping within the vein using the same catheter. In 20 patients with documented clinical episodes of atrial flutter, cavotricuspid isthmus ablation was performed using the current standard technique [12].

Follow-up

An echocardiogram was performed immediately after the procedure, to exclude the presence of pericardial effusion, and 1 or 2 days later. All patients underwent in hospital ECG telemetry monitoring for 72 h. Recurrent sustained AF was treated either by pharmacological (IV flecainide) or electrical cardioversion. All but six patients were discharged in stable sinus rhythm. A transtelephonic ECG recorder was given to all patients to obtain daily ECGs and to allow documentation in case of palpitations for 8 weeks. A standard 12 lead ECG was routinely recorded at 1 week and 1, 3, 6, 9 and 12 months after hospital discharge and

| Table 1 Population characteristics according to clinical presentation |
|-------------------|-------------------|-------------------|
| Variable          | All population (234 pts) | Paroxysmal AF (183 pts) | Persistent AF (51 pts) |
| No heart disease  | 124 (53%)          | 108 (59%)          | 16 (31%)             |
| Arterial hypertension | 71 (30%)          | 53 (29%)          | 18 (35%)             |
| Diabetes mellitus | 10 (4.2%)          | 10 (5.4%)         | 0                    |
| Coronary artery disease | 15 (6.4%)       | 8 (4.3%)          | 7 (14%)              |
| Dilated cardiomyopathy | 5 (2.1%)         | 2 (1.1%)          | 3 (5.8%)             |
| Mitral regurgitation | 20 (8.5%)         | 16 (8.7%)         | 4 (7.8%)             |
| Aortic valvular disease | 3 (1.3%)         | 1 (0.5%)          | 2 (3.9%)             |
| Hyperthyroidism | 9 (3.8%)          | 5 (2.7%)          | 4 (7.8%)             |
| Chronic obstructive pulmonary disease | 5 (2.1%) | 3 (1.6%) | 2 (3.9%) |
| Transient ischaemic attack | 7 (2.9%) | 2 (1%) | 5 (9.8%) |
| Atrial flutter | 20 (8.5%)          | 14 (7.6%)         | 6 (11.7%)            |
| Other arrhythmia | 3 (1.5%)          | 3 (1.6%)          | 0                    |
| PM implant | 7 (2.9%)          | 6 (3.2%)          | 1 (1.9%)             |
| Previous ablation | 6 (2.5%)          | 6 (3.2%)          | 0                    |
| Focal AF | 10 (4.2%)          | 8 (4.3%)          | 2 (3.9%)             |
| Right linear lesions | 12 (5.1%)        | 9 (4.9%)          | 3 (5.8%)             |

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whenever symptoms occurred. A cardiological examination was performed at 1, 3, 6, and 12 months in an outpatient clinic of the ablation centre; at the same time a 24-h Holter recording was obtained in all patients. In patients with stable sinus rhythm, anticoagulants were withdrawn at 2 months in the absence of other risk factors for thromboembolic events, and antiarrhythmic treatment was gradually tapered and discontinued at 4–6 months. The endpoint of the study was considered to be any recurrence, either symptomatic or asymptomatic, of sustained atrial fibrillation or flutter. A repeat catheter ablation procedure was offered to patients with frequent recurrences in spite of antiarrhythmic drug treatment.

Statistical analysis

Continuous variables are expressed as mean ± SD. Continuous variables were compared by Student’s $t$ test, and categorical variables were compared by $\chi^2$ analyses. A Kaplan–Meier analysis with the log-rank test was used to determine the probability of freedom from recurrent AF and the probability of improvement in AF after PV isolation. A Cox

Figure 1  Radiographs in left anterior oblique (LAO) projection showing a circumferential mapping catheter and an ablation catheter positioned at ostia of left superior (Panel A) and left inferior (Panel B) PV. On the right are examples of ostial isolation of the two veins. Electrograms are (from top to bottom) surface leads I, aVF, V1 and V6, ablation catheter at PV ostium, Lasso bipoles 1/2 to 10/1, distal (1/2) to proximal (9/10) bipoles from coronary sinus catheter. Paper speed 100 mm/s. Electrograms are recorded during fixed pacing from distal coronary sinus bipoles before and after ablation of left upper PV (Panel A) and of left inferior PV (Panel B). Ablation resulted in entrance conduction block with disappearance of all PV potentials.
Multivariate regression analysis was performed to determine the clinical predictors of freedom from symptomatic AF. A $P$ value $\leq 0.05$ was considered statistically significant.

**Results**

**Acute results**

Two hundred and sixty-three procedures were performed in 234 patients with a mean of 1.14/patient (four patients had had a prior PV isolation at another Institution). In 19 patients (19/234, 8.1%) the left superior and inferior pulmonary veins had a common ostium, while right superior and inferior pulmonary veins had a common ostium in nine (9/234, 3.8%) patients. Successful disconnection of all targeted PVs was achieved in 90% of cases (236/263). Success rate increased to 98% in the last year as the experience with the procedure increased; no statistically significant difference was observed between successful disconnection rate in paroxysmal (185/204, 91%) and persistent AF patients (51/59, 86%). There was a significant decrease in the total procedure and fluoroscopy time as the experience with the procedure increased; in the last 100 ablations the mean procedure time was 210 ± 86 min and mean fluoroscopy time 46 ± 35 min in comparison with

![Figure 2](https://academic.oup.com/europace/article-abstract/7/2/95/557944/17290557944)
the first 100 ablations where the mean procedure time was 300 ± 108 min and mean fluoroscopy time 64 ± 41 min.

**Acute complications**

An artero-venous fistula at the site of venous puncture occurred in eight patients, requiring surgical correction in four. A venous thrombosis occurred in two patients and required a prolongation of anticoagulation therapy with heparin and warfarin. During a repeat procedure a cerebellar stroke occurred; following medical management the patient made a full recovery without long-term sequelae. There were three cases (1%) of cardiac tamponade requiring pericardiocentesis; minor pericardial effusion followed by spontaneous resolution occurred in 12 patients.

**Early recurrences**

After the procedure all patients were observed by continuous telemetry for 72 h. During this time, an early recurrence of sustained atrial fibrillation occurred in 62/263 (23.6%); early recurrence of AF (ERAF) was higher in persistent (27.2%) than in paroxysmal (21.5%); AF patients ($P = ns$) and was unrelated to the result of the acute procedure, being documented in 32% of patients with incomplete PV isolation and in 22% of those with complete isolation ($P = ns$). Restoration of sinus rhythm was obtained with pharmacological cardioversion in 19 patients, while in the remaining 41 electrical cardioversion was required. In three patients, a second recurrence of sustained atrial fibrillation required further electrical cardioversion.

**Medical treatment following catheter ablation**

All 51 patients with persistent AF were discharged on amiodarone (200 mg/day). Patients with paroxysmal AF were discharged without antiarrhythmic therapy if all PVs were disconnected: oral flecainide was prescribed if one or more veins could not be disconnected (18 patients) or due to the occurrence of atrial ectopy, sustained or non-sustained AF on the day following the procedure. All paroxysmal or persistent AF patients with an episode of sustained AF during the first 48 h following ablation (ERAF) who were not already receiving antiarrhythmic therapy were treated with a class 1c drug. Among 183 patients with paroxysmal AF, 126 (69%) were discharged with antiarrhythmic therapy: class 1c drug in 98 cases, beta-blocker in 17 cases; combination of class 1c drug and beta-blocker in 11 cases.

All patients were treated with oral anticoagulation to maintain INR values between 2 and 3.

**Follow-up**

Following the procedure, the rate of stable sinus rhythm maintenance was, according to the Kaplan–Meier actuarial analysis, 85% at 1 month, 74%, 72% and 65% at 3, 6 and 12 months, respectively. The one year rate of sinus rhythm maintenance was significantly higher among patients with paroxysmal compared with those having persistent atrial fibrillation (68% vs. 54%, $P$ 0.008, Fig. 3). At a mean follow-up of 13 months (range 4–33) the arrhythmia recurred in 74 (28%) patients, 49/204 (24%) with paroxysmal and 25/59 (43%) with persistent AF. Recurrences were documented by daily trans-telephonic ECG (53/74 pts, 71%), by ECGs recorded at the Emergency Room because of symptomatic recurrences (16/74 pts, 22%) or by routine Holter recordings (5/74 pts, 7%); overall, asymptomatic episodes accounted for 17% of the recurrences within the first 8 weeks. Clinical variables, such as age (< or > 50 years, sex, structural heart disease, hypertension, mitral valve disease) were not found, on multivariate analysis, to be predictive of long-term outcome. On the other hand, cumulative arrhythmia free survival rates were significantly higher among patients with disconnection of all pulmonary veins compared with those in whom persistent venoatrial conduction at one or more veins (Fig. 4) persisted.

At 1-month follow-up, all patients in sinus rhythm were taking anticoagulant therapy and

**Figure 3** Kaplan–Meier analysis of one-year arrhythmia-free survival according to the clinical presentation of atrial fibrillation (paroxysmal vs. persistent).
71% were on antiarrhythmic drugs; at one year 7% were on anticoagulant therapy and 29% on antiarhythmic treatment. The persistence of sinus rhythm was higher in paroxysmal AF patients without ERAF; on the other hand, ERAF did not affect outcome among persistent AF patients. No significant difference was observed in the recurrence rate between patients with the PV isolation performed with a conventional or with an irrigated-tip ablation catheter. Patients younger than 55 years, with lone atrial fibrillation or well-controlled hypertension, and a history of atrial fibrillation that had worsened in the last year, had a better outcome, with maintenance of sinus rhythm of 80% at 6 months follow-up (Fig. 5). Overall 74 patients (49 paroxysmal AF, 25 persistent AF) had arrhythmia recurrence of AF. In 51 (69%) of these patients the first ablation attempt was acutely successful, defined as disconnection of all targeted PVs. Among these patients, a repeat procedure was performed in 33 after a period of 17 ± 17 weeks. Recurrence of venoatrial conduction in at least two veins was documented in all; specifically conduction recurred in 26/33 (79%) left superior PVs, 21/26 (81%) left inferior PVs, 28/33 (85%) right superior PVs, and in 17/22 (77%) right inferior PVs. Recurrence of conduction in previously disconnected PVs was similar among paroxysmal and persistent AF patients. The second procedure was acutely successful in all patients. After a mean follow-up of 22 ± 19 weeks, AF recurred in five patients (22%).

Late complications

High grade (70–90%) PV stenosis was documented in three patients undergoing a repeat procedure. Two of them had experienced effort dyspnoea and required angioplasty and stenting of the left and right superior veins. Following the intervention, symptoms subsided in both. No significant difference was observed in the appearance of PV stenosis between conventional or irrigated ablation catheters.

Discussion

Main findings

Segmental ostial ablation guided by circumferential mapping was the technique used in this study because it offered the most straightforward electrophysiological endpoint to guide the electrical disconnection of the pulmonary veins. Our data show that the long-term rate of maintenance of sinus rhythm was significantly higher in those patients in whom complete disconnection of all the veins was achieved compared with those with an incomplete result. Furthermore, the electrophysiological evaluation of patients undergoing a repeat procedure for frequent arrhythmia recurrences invariably showed resumption of atrovenous conduction of one or more veins. These data stress the critical role of the PVs in triggering atrial fibrillation, particularly in those patients with paroxysmal arrhythmia, and suggest that the complete and permanent disconnection of all the PVs from the left atrium should be the minimal endpoint of an ablation procedure for paroxysmal atrial fibrillation. This point has been also demonstrated by the high recurrence rate of AF in
patients intentionally submitted to more limited ablation approaches, involving a multistage approach where the initial intervention aimed at the disconnection of only the superior veins [13]. An alternative ablation protocol has been developed, aimed at delivering point-by-point radiofrequency lesions in the ostial tissue proximal to the venous ostia (PV encircling) [14]. Although this approach does not allow the recognition of a clearly defined electrophysiological endpoint, comparative studies have shown that the anatomically guided PV encircling procedure yields significantly superior sinus rhythm maintenance rates than the electrophysiologically guided segmental ostial PV isolation approach [15]. The long-term outcomes following linear ablation, however, are not uniformly reproducible. According to Ernst et al., the AF recurrence rate following anatomically guided PV isolation associated with linear lesion joining the isolated PVs to the mitral annulus is substantially higher than that reported by others [16–18]. These authors were able to prove that the disappearance of high frequency potentials within the isolated PV is a reliable prediction of a favourable outcome, this again stressing that the main issue is the achievement of PV isolation rather than the mapping technique used to guide the procedure. Other factors that potentially contribute to the discrepancy of the long-term outcome reported in different series is the type of ablation catheter, since conventional 4 mm tip, 8 mm tip, and irrigated-tip devices have been adopted in different laboratories. At the moment no clear evidence supporting the superiority of an irrigated-tip catheter is available to settle this matter.

### Long-term outcome in relation to the clinical presentation

Similar to other published series, long-term results following pulmonary vein isolation were significantly better in patients with paroxysmal than persistent atrial fibrillation. Since other mechanisms than the triggers are involved in the maintenance of atrial fibrillation, different ablation protocols involving linear lesions aimed at the exclusion of a wider area of posterior left atrium should probably be used for the treatment of persistent atrial fibrillation. On this point, however, there are no data available supporting the superiority of a defined ablation approach, in view of the great heterogeneity in the long-term outcome and complication rates that have been reported in different series.

### Medical management after catheter ablation

The extent and the time course of the arrhythmia recurrence could be carefully evaluated due to the specific follow-up protocol employed in our study. Of note is the fact that 70% of recurrent events could be documented by daily transthoracic ECG monitoring within 8 weeks of the ablation procedure, and that a substantial percentage of these events were asymptomatic; less than one fourth of recurrences could be documented by ECG recorded in the Emergency Room, due to symptoms, and 7% were occasionally detected during routine Holter recordings and/or scheduled outpatient clinic visits. Overall, more than 17% of the documented recurrences were asymptomatic, this figure highlighting the need for more extensive use of objective means of evaluation of the ablation outcome. Interestingly, the contribution of asymptomatic episodes to the overall number of recurring events in our study is similar to that reported in observational studies or in those investigating the efficacy of new antiarrhythmic drugs for the treatment of atrial fibrillation [19,20]. When considering long-term results after catheter ablation, the issue of asymptomatic AF recurrences is of great relevance to guide properly further treatment with oral anticoagulant and/or antiarrhythmic drugs. Among patients with proven maintenance of stable sinus rhythm, the use of long-term anticoagulation was reduced to 9% with respect to baseline and was mainly related to the presence of risk factors for cerebral embolism unrelated to atrial fibrillation. There were no embolic events over the long-term follow-up, this compares favourably with the 3–4% annual rate observed in the analysis of the pooled data of the PIAF, AFFIRM, RACE and STAF studies [21–26]. Although these data cannot be taken as a proof of the superiority of catheter ablation with respect to antiarrhythmic drugs for the treatment of atrial fibrillation, they do show that the interruption of oral anticoagulation in patients with proven stable sinus rhythm following catheter ablation is not unsafe. A similar pattern of progressive withdrawal from treatment has been observed for antiarrhythmic drugs, which were still being prescribed, at one year, in 27% of the patients.

### Limitations

In this study, the pulmonary veins were evaluated for stenosis only in patients with symptoms suggesting stenosis or in patients undergoing a second
ablation procedure. Therefore, our data may underestimate the true occurrence of this complication (the real incidence in our population is not known). Short and long-term evaluations may also be needed in asymptomatic patients to rule out acute or late stenosis. A final limitation of this study is that only 40% patients with recurrent AF elected to undergo a second ablation procedure. Therefore, the reasons for recurrent AF could not be identified in the remaining cases.

References


