

Long-term follow-up of persistent atrial fibrillation ablation using termination as a procedural endpoint

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Aims

Catheter ablation of long-lasting persistent atrial fibrillation (AF) has been performed with varying results using a combination of different techniques. Whether arrhythmia termination during ablation is associated with an improved clinical outcome is controversial.

Methods and results

In this prospective study, 153 consecutive patients (56 ± 10 years) underwent catheter ablation of persistent AF (25 ± 33 months) using a stepwise approach with the desired procedural endpoint being AF termination. Repeat ablation was performed for patients with recurrent AF or atrial tachycardia (AT) after a 1 month blanking period. A minimum follow-up of 12 months with repeated Holter monitoring was performed. Atrial fibrillation was terminated in 130 patients (85%). There was a lower incidence of AF in those patients in whom AF was terminated during the index procedure compared with those who had not (5 vs. 39% $P < 0.0001$, mean follow-up 32 ± 11 months). Seventy-nine patients underwent repeat procedures: 64/130 in the termination group (6 AF, 58 AT) and 15 in the non-termination group (9 AF, 7 AT). After repeat ablation, sinus rhythm was maintained in 95% in whom AF was terminated compared with 52% in those in whom AF could not be terminated.

Conclusion

Procedural termination of long-lasting AF by catheter ablation alone is associated with an improved outcome.

Keywords

Atrial fibrillation • Catheter ablation

Introduction

Catheter ablation is an effective therapy for paroxysmal atrial fibrillation (AF) and is emerging as a plausible treatment for persistent AF.^{1–5} While the endpoint of electrical pulmonary vein isolation (PVI) is the agreed goal of procedures targeting the PV-left atrial junction in paroxysmal AF,¹ the targets and endpoints of ablation for persistent AF are ill-defined. Nevertheless there is a clear trend for more extensive procedures. Long-lasting persistent AF can be terminated in a varying number of patients depending on the techniques used.^{2,6} Whether this is linked to the extent of ablation only or is associated with an improved clinical outcome

remains controversial.⁷ The purpose of the present prospective study was to evaluate the clinical outcome in consecutive patients who underwent an ablation approach aiming at AF termination.

Methods

The study comprised 153 consecutive patients undergoing catheter ablation for persistent AF (see *Table 1* for baseline characteristics) between January 2003 and July 2006 at our institution. Atrial fibrillation was defined as persistent (sustained beyond 7 days or lasting less than 7 days but necessitating cardioversion) or long-lasting persistent (continuous AF of greater than 1 year duration) according to the

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Table 1 Baseline characteristics of study cohort (n = 153)

Age, years	55.6 ± 10.4
Gender	130 male; 23 female
Persistent AF (%)	71/153 (46)
Long-lasting persistent AF (%)	82/153 (54)
Duration of sustained AF	
Mean	21.8 ± 33.2 months
Median	12 months
Range	1–240 months
Atrial dimensions	
LA parasternal short axis, mm	47 ± 9
LA transverse, mm	45 ± 7
LA longitudinal, mm	61 ± 8
RA transverse, mm	41 ± 7
RA longitudinal, mm	56 ± 8
Structural heart disease (%)	74/153 (48)
Ejection fraction, %	58 ± 14
Amiodarone use (%)	38/153 (25)
Baseline AFCL, ms	151 ± 21

AF, atrial fibrillation; LA, left atrium; RA, right atrium; AFCL, atrial fibrillation cycle length.

HRS/EHRA/ECAS 2007 Consensus Statement on Catheter and Surgical Ablation of AF.¹ All patients were in AF spontaneously at the beginning of the procedure and all had given written informed consent prior to the procedure.

Electrophysiological study

All anti-arrhythmic medications, with the exception of amiodarone ($n = 38$), were discontinued at least five half-lives prior to ablation. All patients were anti-coagulated with warfarin for at least 1 month before the procedure (target International Normalized Ratio 2–3), and therapeutic anti-coagulation was maintained with intravenous or low molecular weight heparin following warfarin discontinuation 3 days prior to the intervention. Transoesophageal echocardiography was performed within 48 h of the procedure to exclude left atrial thrombus. Warfarin was restarted on the day of the procedure and effective anti-coagulation maintained with heparin until the INR was greater than 2.0.

Surface electrocardiogram and bipolar endocardial electrograms (filtered from 30 to 500 Hz) were continuously monitored and stored on a computer-based digital amplifier/recorder system (Labsystem Pro, Bard EP, Lowell, MA).

The following catheters were introduced via the right femoral vein: (i) a deflectable quadripolar or decapolar catheter (2–5–2 mm electrode spacing, Xtrem, ELA Medical, France) positioned within the CS with the distal electrode positioned at 4 o'clock along the mitral annulus in the 30° left anterior oblique radiographic projection; (ii) a 10 pole, fixed-diameter circumferential mapping catheter to guide PVI (Lasso; Biosense-Webster, Diamond Bar, CA), introduced with the aid of a long sheath (Preface multipurpose, Biosense-Webster or SLO, St. Jude, MN, USA) continuously perfused with heparinized saline; (iii) an 3.5 mm irrigated-tip quadripolar ablation catheter (2–5–2 mm inter-electrode spacings, ThermoCool, Biosense-Webster,

Diamond Bar, CA). A single trans-septal puncture was performed in the anteroposterior radiographic position with pressure monitoring. Left atrial access was confirmed by an appropriate atrial pressure waveform and by contrast injection. The circumferential mapping catheter was introduced to the LA via the trans-septal sheath and the sheath withdrawn to the right atrium to facilitate the passage of the ablation catheter to the LA through the same puncture point. Following trans-septal puncture a bolus of 50 IU/kg of heparin was administered and repeated if the ACT was <200 s.

Catheter ablation protocol

The desired procedural endpoint was termination of AF without anti-arrhythmic drugs or electrical cardioversion. A stepwise approach for ablation was performed under fluoroscopic guidance as has been described elsewhere.^{2,8,9} The AFCL is taken throughout the case from the left and right atrial appendages as there are discrete electrograms at these sites, and it is a more accurate measurement than AFCL taken from the CS.⁸ Pulmonary vein isolation was performed with the endpoint of the abolition or dissociation of activities in all PVs. Electrogram-guided ablation was performed at all sites displaying complex electrogram features: continuous electrical activity,¹⁰ complex rapid and fractionated electrograms, a gradient of activation (a temporal gradient of at least 70 ms between the distal and proximal bipoles on the roving distal ablation electrode), potentially representing a local circuit. The endpoint of electrogram-guided ablation was transformation of complex fractionated electrograms into discrete electrograms and slowing of local cycle length compared with LA appendage cycle length or elimination of electrograms if near the site of a proposed linear lesion. Linear ablation was performed if AF persisted following the previous steps by first targeting the LA roof and later the mitral isthmus with the endpoint of significant reduction or abolition of local electrograms. Following restoration of sinus rhythm, further ablation was performed at these sites as needed to achieve bidirectional conduction block.^{11,12}

The right atrium and superior vena cava were targeted for ablation if AF persisted after the previous steps. Linear ablation was performed in all patients at the cavotricuspid isthmus either before or after restoration of sinus rhythm and bidirectional conduction block confirmed.

Termination of AF was defined as a transition directly from AF to sinus rhythm or via one or more intermediate atrial tachycardias (ATs). Atrial fibrillation was defined by beat-to-beat variability in cycle length and morphology, while AT was defined as an organized atrial rhythm with a stable cycle length, a consistent endocardial activation sequence in both atria and a monomorphic P wave. Atrial tachycardia was described as focal if centrifugal activation could be demonstrated from a single atrial region. Macroreentry was defined by sequential mapping of the entire tachycardia cycle length within one chamber and consistent entrainment manoeuvres. Activation mapping and catheter ablation of these tachycardias was performed until restoration of sinus rhythm without the routine use of three dimensional electro-anatomical tools. Anti-arrhythmic medication was not administered during the procedure in any patient to facilitate AF termination.

Radiofrequency ablation was performed in temperature-control mode with a target tissue temperature of not more than 45°C. Powers of 25–40 W were used with manual titration of the saline perfusate from 10 to 60 mL/min to achieve the desired power. The power was limited to 30 W on the posterior wall and 25 W within the CS. Ablation was preferentially performed with the distal electrode parallel to the target atrial tissue rather than perpendicular so as to minimize the risk of steam popping.

Predictive factors for atrial fibrillation termination

The following patient and procedural variables were evaluated in association with AF termination by ablation: patient age, sex, presence of structural heart disease, duration of persistent AF, LA dimension, LV ejection fraction, baseline AF cycle length, use of amiodarone, duration of procedure, peak troponin release and duration of radiofrequency energy application. For AFCL, the cycle length of local activity was recorded in the left and right atrial appendages before and after each ablation step for 30 s and the mean AFCL calculated using custom software as previously described and validated. Interelectrogram intervals of <100 ms or continuous electrical activity were manually corrected to count as a single interval however the electrograms within the appendages are usually unfractionated and of high amplitude (0.5–2.0 mV) thereby facilitating unambiguous automatic annotation.

Follow-up

Patients were routinely hospitalized for up to 5 days post-procedure and again for 1 day at 1, 3, 6, and 12 months for clinical interview and ambulatory monitoring in addition to later routine follow-up by the referring cardiologist including Holter monitoring in the event of symptoms. Recurrence of atrial arrhythmia within the first month only was considered transient¹³ and a blanking period of 4 weeks was applied. Transthoracic echocardiography and exercise stress testing were performed at 6 months. Anti-arrhythmic medication was continued for 1–3 months following the index procedure and warfarin anti-coagulation was continued for at least 6 months. A repeat ablation procedure was undertaken in the event of a recurrence of AF or AT whether symptomatic or not.

All patients were personally contacted for updated follow-up in January 2008. In addition, during the same month 32 patients selected at random from the Bordeaux region underwent 10 day ambulatory monitoring. Success was defined with and without anti-arrhythmic drugs as the absence of all documented arrhythmia or symptoms suggestive of an arrhythmia recurrence.

Statistical analysis

Based upon a prior study,¹⁴ we estimated the sample sizes from an event rate of 40% compared with 10%, with a power of 80%, and two-sided 5% significance test, the NNTT = 25 patients per group.

Continuous variables are reported as mean \pm standard deviation or median (and range). Comparison between groups was performed with the Student's *t*-test or the Wilcoxon Rank-Sum test (non-normally distributed data). Categorical variables are reported as number and percentage and were compared using the Fisher's exact test. For the stepwise logistic regression analysis, the continuous variables were appropriately transformed where required to render them normally distributed. All tests were two-tailed and statistical significance was established at $P < 0.05$. Cumulative event rates (AF recurrence, arrhythmia recurrence, and AT recurrence) were calculated according to the Kaplan–Meier method.

Results

Mode and sites of atrial fibrillation termination

In 130 of 153 patients (85%), AF was terminated by catheter ablation alone while in the remaining 23 patients (15%) AF could not be terminated by ablation and required pharmacological and/or DC cardioversion. The mean procedure, fluoroscopy, and radiofrequency energy delivery durations were 255 ± 69 min, 86 ± 28 min, and 88 ± 27 min, respectively, for the whole population.

In the non-termination group there was a trend toward longer procedural times compared with those in whom AF was terminated (280 ± 84 vs. 250 ± 65 min, $P = 0.07$) and a longer duration of RF delivery (97 ± 31 vs. 87 ± 26 min, $P = \text{NS}$, Table 2), reflecting the continuation of ablation of complex electrograms in the non-termination group in both atria. However, there was no significant difference in peak troponin release between the termination group and the non-termination group (median 9.65, IQ range 6.1–15.0 vs. 13.4, 7.5–14.5 ng/mL; $P = 0.45$).

In 14/130 patients (11%), the pulmonary veins were the site of AF termination; in 89 patients (68%), AF terminated during the phase of electrogram-guided ablation; AF terminated in the remaining 27 patients (21%) during linear ablation. Overall, AF was terminated in the LA in 118 patients (91%) and in the right atrium in the remaining 12 patients (9%). Of 130 patients in whom AF terminated during

Table 2 Comparison of baseline and procedural parameters in patients where AF could (termination) and could not (no termination) be terminated directly by catheter ablation

	Termination	No termination	P-value
Median LLA duration (months)	12 (1–131)	24 (3–240)	0.0022 ^a
LA dimension (mm)	47 \pm 8	52 \pm 10	0.030 ^a
Ejection fraction (%)	58 \pm 14	59 \pm 15	0.387
Baseline AFCL (ms)	154 \pm 21	138 \pm 15	0.0012 ^a
Amiodarone use (n)	36/130	2/23	0.066
Peak troponin (μ g/L)	10.8 \pm 6.6	12.0 \pm 4.9	0.45
Median	9.65	13.4	
IQ range	6.1–15.0	7.5–14.5	
Procedure time (min)	250 \pm 65	280 \pm 84	0.0737
RF duration (min)	87 \pm 26	97 \pm 31	0.244

LLAF, long-lasting atrial fibrillation; LA, left atrium; AFCL, atrial fibrillation cycle length; RF, radiofrequency.

^aVariables selected for multivariate analysis.

Table 3 Breakdown of anatomical sites of termination of atrial fibrillation by catheter ablation

Site of AF termination	Number of patients
Left atrium (n = 118)	
Inferior LA	11
CS os	2
CS (epicardial)	17
Left atrial appendage	25
Mitral isthmus	17
Pulmonary veins	14
Interatrial septum	12
Roof	8
Posterior LA	6
Anterior LA	4
Lateral LA	2
Right atrium (n = 12)	
Right atrial appendage	4
Intercaval	3
Cavotricuspid isthmus	2
Superior vena cava	2
Foramen ovale	1

LA, left atrium; AF, atrial fibrillation.

ablation, 115 underwent ablation within the CS during the procedure. A breakdown of the anatomical sites at which AF terminated during ablation is presented in Table 3.

Factors associated with atrial fibrillation termination

Of the patients in whom AF terminated during catheter ablation, 108 (83%) terminated via an intermediate step of AT and the remaining 22 (17%) converted directly from AF to sinus rhythm, with no statistical distinction between the two groups with respect to AF duration or baseline AFCL. The characteristics of patients in whom AF could and could not be terminated are shown in Table 2.

Using a stepwise logistical regression technique incorporating age, duration of AF, ejection fraction, LA parasternal dimension, baseline AFCL, procedure duration and RF energy delivery duration, termination of AF during the index procedure is statistically associated with a smaller LA dimension, a shorter duration of persistent AF and a longer AFCL at baseline. Termination of AF could be reliably predicted and increased in likelihood with decreasing duration of AF (Figure 1). In patients having persistent AF lasting less than 48 months the AFCL was a strong predictor of successful AF termination with a longer AFCL associated with a greater likelihood of termination (Figure 2).

Arrhythmia recurrence and mode of atrial fibrillation termination

Atrial fibrillation was terminated in 130 patients (85%), directly to sinus rhythm in 22 patients or via ablation of intermediate AT in

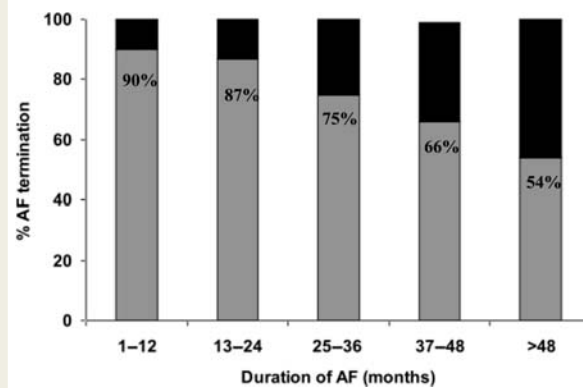


Figure 1 Percentage of patients in whom atrial fibrillation was terminated (grey bars) and not terminated (black bars) during the index procedure plotted as a function of the duration of persistent atrial fibrillation prior to the ablation procedure.

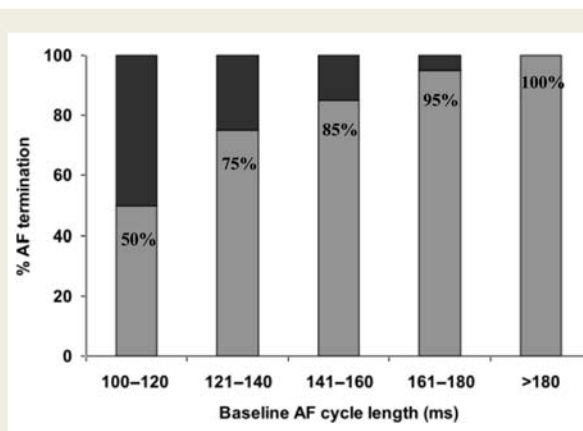


Figure 2 Percentage of patients in whom atrial fibrillation was terminated (grey bars) and not terminated (black bars) during the index procedure plotted as a function of the baseline atrial fibrillation cycle length measured in the left atrial appendage.

108 patients. Atrial fibrillation could not be terminated (Non-Term) by catheter ablation in 23 patients (15%). Seventy-nine patients underwent repeat procedures: 64/130 in the termination group (6 AF, 58 AT) and 15 in the non-termination group (9 AF, 7 AT). Recurrence of AF was documented in only six patients (5%) among the 130 patients in whom AF was terminated by catheter ablation vs. 9 of 23 patients (39%) without AF termination ($P < 0.0001$) (Figure 3). Recurrence of AT was documented in 64 patients (49%) all of whom underwent repeat electrophysiological study; the indication for restudy was AT in 58 patients (91%) and recurrent AF in 6 patients (9%), representing 44 and 5%, respectively, of the patients in whom AF was terminated during the index procedure (Figures 4 and 5).

Among the 23 patients in whom AF could not be terminated by catheter ablation during the index procedure, 16 patients (70%) had a clinical recurrence of arrhythmia and underwent a repeat

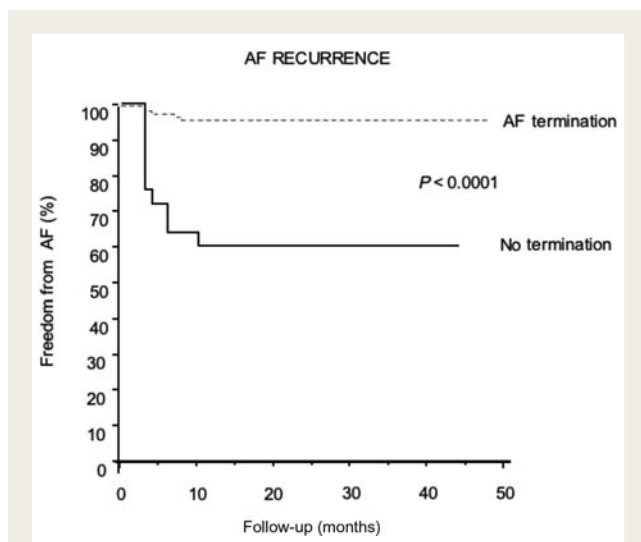


Figure 3 Kaplan–Meier plot demonstrating time to first atrial fibrillation recurrence in patients undergoing catheter ablation for persistent atrial fibrillation according to whether atrial fibrillation was terminated (termination) or not terminated (non-termination) during the ablation procedure.

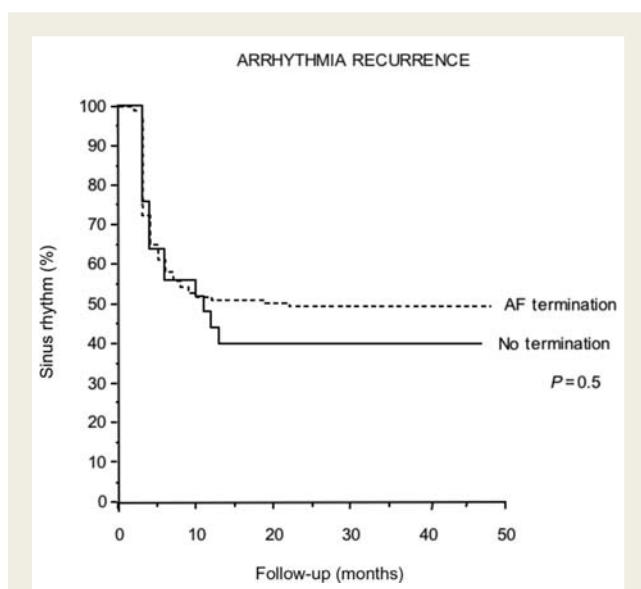


Figure 4 Kaplan–Meier plot demonstrating time to first arrhythmia recurrence in patients undergoing catheter ablation for persistent atrial fibrillation according to whether atrial fibrillation was terminated (termination) or not terminated (non-termination) during the ablation procedure.

electrophysiological study. There were nine (56%) patients with recurrent AF while AT was the indication for restudy in the remaining seven patients (44%). Of the nine patients with AF recurrence who underwent a complete sequential re-ablation procedure, i.e. PVI, electrogram guided and linear ablation, eight required DC cardioversion to terminate AF. Five of seven AT

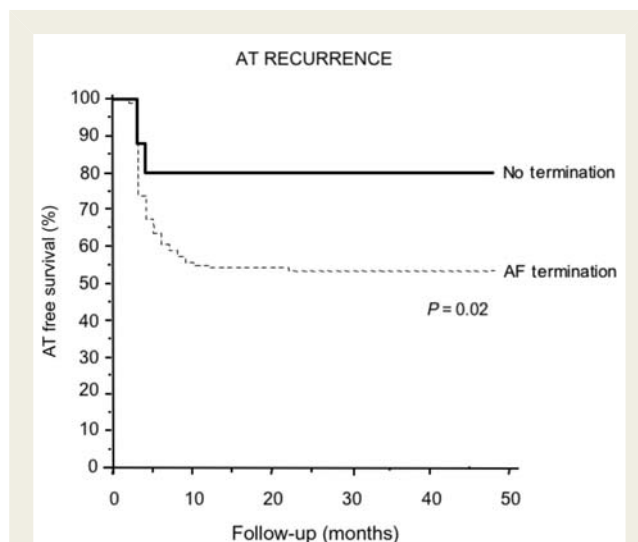


Figure 5 Kaplan–Meier plot demonstrating time to first atrial tachycardia recurrence in patients undergoing catheter ablation for persistent atrial fibrillation according to whether atrial fibrillation was terminated (termination) or not terminated (non-termination) during the ablation procedure.

recurrences were successfully mapped and ablated while two were unidentified and were treated by DC cardioversion and completion of conduction block at the PVs and previously ablated linear lesions (Figure 6) (Table 4).

Adverse effects

There were six complications in this study, all of which were treated conventionally with no long-term sequelae (two tamponade, two femoral haematomas, and two reversible right phrenic nerve injuries).

Atrial fibrillation termination and long-term follow-up

At a median of 34 months (range 28–40) of follow-up for the study cohort, 124/130 patients (95%) in the AF Termination group are in stable sinus rhythm after the last procedure. The incidence of sinus rhythm was significantly lower in the AF Non-Termination group (12/23 patients, 52%; $P < 0.001$, Figure 3).

In the AF Termination group, of the six patients with persisting arrhythmia at follow-up, one patient is in persistent AF, one patient has a persistent, slow AT with which he is asymptomatic, and four patients have paroxysmal AT. In the AF Non-Termination group, six patients remain in persistent AF, three patients have paroxysmal AF, and two have paroxysmal AT. In the subset of patients from the Bordeaux region who underwent long-term monitoring, the results confirmed the Holter monitoring, and surprisingly there were no episodes of asymptomatic AF.

In the AF termination group, 89% of patients have discontinued all anti-arrhythmic drugs and warfarin while in the AF Non-

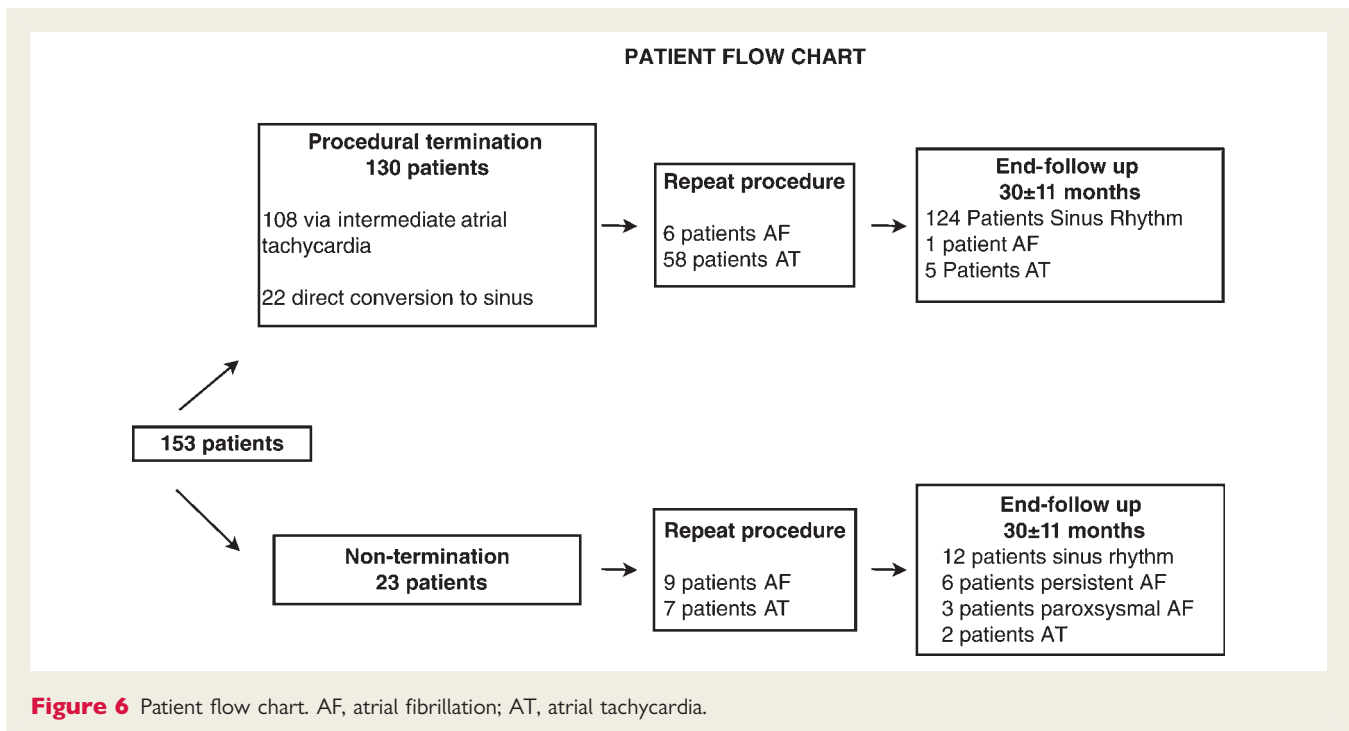


Table 4 Sites and mechanisms of atrial tachycardia during the follow-up period in 80 patients who underwent a repeat procedure for arrhythmia recurrence

Site of AT	Termination		No termination	
	Reentrant	Focal	Reentrant	Focal
Macroreentry				
Mitral annulus	28	2	2	0
LA roof	16	1	3	0
CTI	7	1	1	0
Localized reentry				
Anterior LA	2	2	0	0
Foramen ovale	7	0	0	0
Septum	5	4	0	1
Inferior LA	0	2	0	0
LAA	1	3	2	0
CS	1	8	0	0
SVC	1	2	0	0
PV	0	8	0	2
Posterior LA	0	1	0	0
RA	0	2	0	0
Total	68	36	8	3

LA, left atrium; CTI, cavotricuspid isthmus; SVC, superior vena cava; PV, pulmonary vein; RA, right atrium; AT, atrial tachycardia.

'Termination' and 'no termination' refer to those patients in whom atrial fibrillation was terminated and not terminated by ablation in the index procedure, respectively.

Termination group, only 25% of patients have discontinued anti-arrhythmic drugs and warfarin.

Discussion

This study demonstrates that successful AF termination is associated with a better clinical outcome.

The appropriate endpoint for atrial fibrillation ablation

Atrial fibrillation is a mechanistically heterogeneous arrhythmia. At its simplest, a single, rapidly and episodically discharging focus located within a discrete structure, often a pulmonary vein, can initiate AF which can be subsequently terminated by elimination of that identifiable focus using radiofrequency energy.¹⁵ Long-lasting persistent AF is a complex arrhythmia; termination frequently requires targeting thoracic veins^{4,16} and large areas of both atria to incorporate complex-fractionated atrial electrograms (CFAE)^{15,17} and linear lesions.^{11,12,18–23}

In persistent AF it is often difficult to decide when the procedure should terminate. Endpoints for ablation targeting CFAE may include voltage reduction, organization,² or elimination of fractionated activity,¹⁵ all of which are somewhat subjective in nature, while linear ablation is deemed complete when bidirectional conduction block can be demonstrated by pacing manoeuvres.¹ Inducibility testing is of little use in patients with long-lasting persistent AF as this invariably results in re-induction of AF.² There can be no ambiguity about sinus rhythm as an endpoint for catheter ablation but to date, there have been no clinical outcome data evidence to support this endpoint and thereby justify the lengthy and difficult procedures required to achieve it.

Termination of atrial fibrillation as an endpoint

In the present study, sinus rhythm was restored by catheter ablation in 85%. Termination of AF has been reported in different studies with variable results.^{6,7,24} Nademanee *et al.*¹⁵ reported a high rate of AF termination using an electrogram-based approach. The present prospective study reports the long-term outcome when such an endpoint is employed. In those patients in whom sinus rhythm was restored during the index procedure, the long-term freedom from AF was considerably greater (recurrence of AF in only 5%) than those patients in whom sinus rhythm was not restored. Why should restoration of sinus rhythm be associated with an improved clinical outcome? Termination of AF could be interpreted as a complete suppression of all AF initiating and perpetuating mechanisms active 'at that time in that patient'.

However, almost half of the patients (45%) in whom AF has been terminated return with AT, which is the main limitation of this approach. This suggests that the initial ablation procedure results in a permanent modification of the atrial electrophysiological substrate such that fibrillation could no longer occur. The higher incidence of tachycardia recurrence than that reported by other groups with widespread LA ablation^{25–27} may be a proarrhythmic consequence of the anatomically disparate electrogram-guided lesions which are needed to terminate AF, analogous to the proarrhythmic effect of incomplete PVI⁵ or linear lesions^{28,29} in more conventional ablation lesion sets. Surprisingly, 20% of recurrent ATs occurred at sites that had not been previously targeted for ablation. In the reentrant cases, this may reflect the creation of critical isthmus regions between ablation targets. For example, perimitral reentry could be promoted by an isthmus lying between the lateral aspect of the inferior LA lesion and anterior aspect of the encircling lesion around the left PVs. The focal tachycardias may represent non-pulmonary venous triggers which were not manifest during the index procedure but which have been previously well described.³⁰

Importantly it should be emphasized that termination of AF was not a stand-alone endpoint of the ablation approach. Pulmonary vein isolation and integrity of linear lesions was confirmed or completed by further ablation as necessary following restoration of sinus rhythm.

Predictors of atrial fibrillation termination by ablation

Multivariate logistic regression analysis demonstrates AFCL and duration of AF as the factors independently associated with AF termination in the index procedure. In the present study, termination of AF by catheter ablation is more easily achieved in those patients with a shorter history of AF, a smaller LA dimension, and a longer baseline AFCL, measured in the LAA.

The AFCL has been shown to be a clinically useful tool to track procedural progress and has been shown to prolong prior to AF termination in both paroxysmal and persistent AF treated by ablation a finding which is further supported by this study. Computer modelling of human AF has demonstrated it to reflect also the number of elements participating in the fibrillatory process;³¹ therefore a shorter AFCL reflects a short refractory period and

higher number of perpetuating activities, both of which are characteristic of long-lasting AF.

Limitations

Although this was a prospective study, with a desired endpoint of procedural termination, it is impossible to randomize patients to either termination or non-termination. Additionally, had we attempted to achieve non-termination this would inevitably have meant less ablation, but then the problem lies in assessing what is the procedural endpoint to ensure non-termination. Asymptomatic recurrences of AF are common and although all patients underwent regular clinical interview with their referring cardiologist in addition to attending the ablation centre at prescribed intervals for follow-up and 24 h Holter recording, this is unlikely to be as effective in detecting all asymptomatic episodes as are longer recording periods.³² This is an inherent limitation in all AF studies without implantable devices. However, in a subgroup of patients with long-term monitoring, surprisingly there were no asymptomatic recurrences.

Although restoration of sinus rhythm requires long procedures and extensive ablation with significant damage confirmed by electroanatomical mapping work, a previous study demonstrated recovery of atrial contractile function in 98% of patients in sinus rhythm at 6 months follow-up.³³

When performing electrogram-targeted ablation, the features were assessed visually and without the need for electroanatomical mapping systems with specialized software for detecting fractionation, as this has been shown to be effective in previous studies, and is seen as the gold standard.^{15,17,34,35}

Lastly, this study did not compare the effect of termination of AF alone with restoration of sinus rhythm following conversion from AF to AT as procedural endpoints.

Conclusions

Termination of persistent AF by catheter ablation is associated with a better long-term clinical outcome than when AF is not terminated.

Conflict of interest: none declared.

References

1. Calkins H, Brugada J, Packer DL, Cappato R, Chen SA, Crijns HJ, Damiano RJJ, Davies DW, Haines DE, Haissaguerre M, Iesaka Y, Jackman W, Jais P, Kottkamp H, Kuck KH, Lindsay BD, Marchlinski FE, McCarthy PM, Mont JL, Morady F, Nademanee K, Natale A, Pappone C, Prystowsky E, Raviele A, Ruskin JN, Shemin RJ. HRS/EHRA/ECAS Expert Consensus Statement On Catheter Surgical Ablation Of Atrial Fibrillation: Recommendations For Personnel, Policy, Procedures And Follow-Up. A Report Of The Heart Rhythm Society (HRS) Task Force On Catheter And Surgical Ablation Of Atrial Fibrillation. *Heart Rhythm* 2007;**4**:816–861.
2. Haissaguerre M, Sanders P, Hocini M, Takahashi Y, Rotter M, Sacher F, Rostock T, Hsu LF, Bordachar P, Reuter S, Roudaut R, Clementy J, Jais P. Catheter ablation of long-lasting persistent atrial fibrillation: critical structures for termination. *J Cardiovasc Electrophysiol* 2005;**16**:1125–1137.
3. Kanagaratnam L, Tomassoni G, Schweikert R, Pavia S, Bash D, Beheiry S, Lesh M, Niebauer M, Saliba W, Chung M, Tchou P, Natale A. Empirical pulmonary vein isolation in patients with chronic atrial fibrillation using a three-dimensional non-fluoroscopic mapping system: long-term follow-up. *Pacing Clin Electrophysiol* 2001;**24**:1774–1779.
4. Oral H, Pappone C, Chugh A, Good E, Bogun F, Pelosi FJ, Bates ER, Lehmann MH, Vicedomini G, Augello G, Agricola E, Sala S, Santinelli V, Morady F.

- Circumferential pulmonary-vein ablation for chronic atrial fibrillation. *N Engl J Med* 2006;**354**:934–941.
5. Ouyang F, Antz M, Ernst S, Hachiya H, Mavrakis H, Deger FT, Schaumann A, Chun J, Falk P, Hennig D, Liu X, Bansch D, Kuck KH. Recovered pulmonary vein conduction as a dominant factor for recurrent atrial tachyarrhythmias after complete circular isolation of the pulmonary veins: lessons from double Lasso technique. *Circulation* 2005;**111**:127–135.
 6. Oral H, Chugh A, Good E, Crawford T, Sarrazin JF, Kuhne M, Chalfoun N, Wells D, Boonyapisit W, Gutela N, Sankaran S, Kfahagi A, Jongnarangsin K, Pelosi F, Bogun F, Morady F. A randomized evaluation of right atrial ablation after left atrial ablation of complex fractionated electrograms for long lasting persistent atrial fibrillation. *Circ Arrhythm Electrophysiol* 2008;**1**:6–13.
 7. Elayi IS, Arruda M, Di Biase L, Ching CK, Patel D, Kanj MH, Fahmy TS, Khan MN, Meulet JE, Barrett C, Philips KP, Wasson S, Civello KC, Bailey SM, Zakaib J, Callahan T, Cummings JE, Burkhardt JD, Martin DO, Bhargava M, Dresing T, Schweikert RA, Wazni OM, Saliba W, Natale A. Is atrial fibrillation termination mode during ablation for permanent AF a predictor of long term maintenance of sinus rhythm? (Abstract). *Heart Rhythm* 2007;**4**:S320.
 8. O'Neill MD, Jais P, Takahashi Y, Jonsson A, Sacher F, Hocini M, Sanders P, Rostock T, Rotter M, Pernat A, Clementy J, Haissaguerre M. The stepwise ablation approach for chronic atrial fibrillation—evidence for a cumulative effect. *J Interv Card Electrophysiol* 2006;**16**:153–167.
 9. Takahashi Y, O'Neill MD, Hocini M, Reant P, Jonsson A, Jais P, Sanders P, Rostock T, Rotter M, Sacher F, Laffite S, Roudaut R, Clementy J, Haissaguerre M. Effects of stepwise ablation of chronic atrial fibrillation on atrial electrical and mechanical properties. *J Am Coll Cardiol* 2007;**49**:1306–1314.
 10. Takahashi Y, O'Neill MD, Hocini M, Dubois R, Matsuo S, Knecht S, Mahapatra S, Lim KT, Jais P, Jonsson A, Sacher F, Sanders P, Rostock T, Bordachar P, Clementy J, Klein GJ, Haissaguerre M. Characterization of electrograms associated with termination of chronic atrial fibrillation by catheter ablation. *J Am Coll Cardiol* 2008;**51**:1003–1010.
 11. Hocini M, Jais P, Sanders P, Takahashi Y, Rotter M, Rostock T, Hsu LF, Sacher F, Reuter S, Clementy J, Haissaguerre M. Techniques, evaluation, and consequences of linear block at the left atrial roof in paroxysmal atrial fibrillation: a prospective randomized study. *Circulation* 2005;**112**:3688–3696.
 12. Jais P, Hocini M, Hsu LF, Sanders P, Scavee C, Weerasooriya R, Macle L, Raybaud F, Garrigue S, Shah DC, Le Metayer P, Clementy J, Haissaguerre M. Technique and results of linear ablation at the mitral isthmus. *Circulation* 2004;**110**:2996–3002.
 13. Oral H, Knight BP, Tada H, Ozaydin M, Chugh A, Hassan S, Scharf C, Lai SW, Greenstein R, Pelosi FJ, Strickberger SA, Morady F. Pulmonary vein isolation for paroxysmal and persistent atrial fibrillation. *Circulation* 2002;**105**:1077–1081.
 14. Haissaguerre M, Hocini M, Sanders P, Sacher F, Rotter M, Takahashi Y, Rostock T, Hsu LF, Bordachar P, Reuter S, Roudaut R, Clementy J, Jais P. Catheter ablation of long-lasting persistent atrial fibrillation: clinical outcome and mechanisms of subsequent arrhythmias. *J Cardiovasc Electrophysiol* 2005;**16**:1138–1147.
 15. Nademanee K, McKenzie J, Kosar E, Schwab M, Sunsaneewitayakul B, Vasavakul T, Khunnawat C, Ngarmukos T. A new approach for catheter ablation of atrial fibrillation: mapping of the electrophysiologic substrate. *J Am Coll Cardiol* 2004;**43**:2044–2053.
 16. Kanj MH, Wazni O, Fahmy T, Thal S, Patel D, Elay C, Di Biase L, Arruda M, Saliba W, Schweikert RA, Cummings JE, Burkhardt JD, Martin DO, Pelargonio G, Dello Russo A, Casella M, Santarelli P, Potenza D, Fanelli R, Massaro R, Forleo G, Natale A. Pulmonary vein antral isolation using an open irrigation ablation catheter for the treatment of atrial fibrillation: a randomized pilot study. *J Am Coll Cardiol* 2007;**49**:1634–1641.
 17. Oral H, Chugh A, Good E, Wimmer A, Dey S, Gadeela N, Sankaran S, Crawford T, Sarrazin JF, Kuhne M, Chalfoun N, Wells D, Frederick M, Fortino J, Benloucif-Moore S, Jongnarangsin K, Pelosi FJ, Bogun F, Morady F. Radiofrequency catheter ablation of chronic atrial fibrillation guided by complex electrograms. *Circulation* 2007;**115**:2606–2612.
 18. Willems S, Klemm H, Rostock T, Brandstrup B, Ventura R, Steven D, Rissius T, Lutomsky B, Meinertz T. Substrate modification combined with pulmonary vein isolation improves outcome of catheter ablation in patients with persistent atrial fibrillation: a prospective randomized comparison. *Eur Heart J* 2006;**27**:2871–2878.
 19. Gaita F, Riccardi R, Caponi D, Shah D, Garberoglio L, Vivalda L, Dulio A, Chiechio A, Manasse E, Gallotti R. Linear cryoablation of the left atrium versus pulmonary vein cryoisolation in patients with permanent atrial fibrillation and valvular heart disease: correlation of electroanatomic mapping and long-term clinical results. *Circulation* 2005;**111**:136–142.
 20. Mandapati R, Skanes A, Chen J, Berenfeld O, Jalife J. Stable microreentrant sources as a mechanism of atrial fibrillation in the isolated sheep heart. *Circulation* 2000;**101**:194–199.
 21. Scherlag BJ, Nakagawa H, Jackman WM, Yamanashi WS, Patterson E, Po S, Lazzara R. Electrical stimulation to identify neural elements on the heart: their role in atrial fibrillation. *J Interv Card Electrophysiol* 2005;**13**(Suppl. 1):37–42.
 22. Haissaguerre M, Hocini M, Sanders P, Takahashi Y, Rotter M, Sacher F, Rostock T, Hsu LF, Jonsson A, O'Neill MD, Bordachar P, Reuter S, Roudaut R, Clementy J, Jais P. Localized sources maintaining atrial fibrillation organized by prior ablation. *Circulation* 2006;**113**:616–625.
 23. Pappone C, Santinelli V, Manguso F, Vicedomini G, Gugliotta F, Augello G, Mazzone P, Tortoriello V, Landoni G, Zangrillo A, Lang C, Tomita T, Mesas C, Mastella E, Alfieri O. Pulmonary vein denervation enhances long-term benefit after circumferential ablation for paroxysmal atrial fibrillation. *Circulation* 2004;**109**:327–334.
 24. Estner HL, Hessling G, Ndrepepa G, Luik A, Schmitt C, Konietzko A, Ucer E, Wu J, Kolb C, Pflaumer A, Zrenner B, Deisenhofer I. Acute effects and long-term outcome of pulmonary vein isolation in combination with electrogram-guided substrate ablation for persistent atrial fibrillation. *Am J Cardiol* 2008;**101**:332–337.
 25. Ouyang F, Ernst S, Chun J, Bansch D, Li Y, Schaumann A, Mavrakis H, Liu X, Deger FT, Schmidt B, Xue Y, Cao J, Hennig D, Huang H, Kuck KH, Antz M. Electrophysiological findings during ablation of persistent atrial fibrillation with electroanatomic mapping and double Lasso catheter technique. *Circulation* 2005;**112**:3038–3048.
 26. Pappone C, Manguso F, Vicedomini G, Gugliotta F, Santinelli O, Ferro A, Gulletta S, Sala S, Sora N, Paglino G, Augello G, Agricola E, Zangrillo A, Alfieri O, Santinelli V. Prevention of iatrogenic atrial tachycardia after ablation of atrial fibrillation: a prospective randomized study comparing circumferential pulmonary vein ablation with a modified approach. *Circulation* 2004;**110**:3036–3042.
 27. Arentz T, Weber R, Burkle G, Herrera C, Blum T, Stockinger J, Minners J, Neumann FJ, Kalusche D. Small or large isolation areas around the pulmonary veins for the treatment of atrial fibrillation? results from a prospective randomized study. *Circulation* 2007;**115**:3057–3063.
 28. Gerstenfeld EP, Marchlinski FE. Mapping and ablation of left atrial tachycardias occurring after atrial fibrillation ablation. *Heart Rhythm* 2007;**4**:S65–S72.
 29. Knecht S, Hocini M, Wright M, Lelouche N, O'Neill MD, Matsuo S, Nault I, Chauhan VS, Makati KJ, Bevilacqua M, Lim KT, Sacher F, Deplagne A, Derval N, Bordachar P, Jais P, Clementy J, Haissaguerre M. Left atrial linear lesions are required for successful treatment of persistent atrial fibrillation. *Eur Heart J* 2008;**19**:2359–2366.
 30. Lin WS, Tai CT, Hsieh MH, Tsai CF, Lin YK, Tsao HM, Huang JL, Yu WC, Yang SP, Ding YA, Chang MS, Chen SA. Catheter ablation of paroxysmal atrial fibrillation initiated by non-pulmonary vein ectopy. *Circulation* 2003;**107**:3176–3183.
 31. Haissaguerre M, Lim KT, Jacquemet V, Rotter M, Dang L, Hocini M, Matsuo S, Knecht S, Jais P, Virag N. Atrial fibrillatory cycle length: computer simulation and potential clinical importance. *Europace* 2007;**9**(Suppl. 6):Vi64–Vi70.
 32. Kottkamp H, Tanner H, Kobza R, Schirdewahn P, Dorszewski A, Gerdts-Li JH, Carbucicchio C, Piorowski C, Hindricks G. Time courses and quantitative analysis of atrial fibrillation episode number and duration after circular plus linear left atrial lesions: trigger elimination or substrate modification: early or delayed cure? *J Am Coll Cardiol* 2004;**44**:869–877.
 33. Takahashi Y, O'Neill MD, Jonsson A, Sanders P, Sacher F, Hocini M, Jais P, Clementy J, Haissaguerre M. How to interpret and identify pulmonary vein recordings with the Lasso catheter. *Heart Rhythm* 2006;**3**:748–750.
 34. Scherr D, Dalal D, Cheema A, Cheng A, Henrikson CA, Spragg D, Marine JE, Berger RD, Calkins H, Dong J. Automated detection and characterization of complex fractionated atrial electrograms in human left atrium during atrial fibrillation. *Heart Rhythm* 2007;**4**:1013–1020.
 35. Verma A, Novak P, Macle L, Whaley B, Beardsall M, Wulffhart Z, Khaykin Y. A prospective, multicenter evaluation of ablating complex fractionated electrograms (Cfegs) during atrial fibrillation (AF) identified by an automated mapping algorithm: acute effects on AF and efficacy as an adjuvant strategy. *Heart Rhythm* 2008;**5**:198–205.