Europace (2011) **13**, 355–361
doi:10.1093/europace/euq434

Predictors of recurrence following radiofrequency ablation for persistent atrial fibrillation

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Received 10 May 2010; accepted after revision 3 November 2010; online publish-ahead-of-print 8 December 2010

Aims To establish clinical factors affecting success in persistent atrial fibrillation (AF) ablation.

Methods and results Wide area circumferential ablation with linear and electrogram-based left atrial (LA) ablation was performed in 191 consecutive patients for persistent AF. After mean follow-up of 13.0 ± 8.9 months, overall success was 64% requiring a mean of 1.5 procedures. Single procedure success rate was 32%. Left atrial size was a univariate predictor of recurrence after a single procedure ($P = 0.04$). Only LA size [hazard ratio (HR) 1.05/mm with 95% confidential interval (CI) 1.02–1.08] was an independent predictor of recurrence after a single procedure. Only LA size was a univariate predictor of recurrence after multiple procedures ($P < 0.01$). Left atrial size (HR 1.07/mm with 95% CI 1.02–1.11) and hypertrophic cardiomyopathy (HCM; HR 2.42 with 95% CI 1.06–5.55) were independent predictors of recurrence after multiple procedures. Ablation strategy did not affect success after a single procedure. Left atrial size of <43 mm predicted long-term success with a sensitivity of 92%, specificity 52%, positive predictive value 49%, and negative predictive value 93%. With LA size >43 mm, HCM (HR 3.09 with 95% CI 1.70–7.5) and AF duration (HR 1.07/year with 95% CI 1.00–1.13) were independent predictors of recurrence.

Conclusion Left atrial size is the major independent determinant of AF recurrence after ablation for persistent AF. This has important implications for patient selection for persistent AF ablation and the evaluation of AF ablation clinical trial results.

Keywords Atrial fibrillation • Left atrium • Catheter ablation

Introduction

Radiofrequency ablation is widely accepted as an effective treatment for paroxysmal atrial fibrillation (PAF), with reported success rates as high as 89%.[1] However, questions remain over the efficacy of ablation in persistent AF, with higher recurrence rates and over the frequent requirement for repeat procedures.[2,3] Single procedure success rates are only 52%, even in the most experienced centres, requiring a mean 1.8 procedures/patient and a mean procedure time of 280 min.[4]

Embarking on a therapeutic ablation journey for patients with persistent AF is a major undertaking requiring frequent hospital visits, long and complex procedures, repeat ablation, and a 2–6% incidence of serious complications per procedure.[4,5]

Previous studies have examined predictors of success following ablation in mixed populations of patients with paroxysmal and persistent AF.[6,7] This is potentially flawed, however, as persistent AF has many differences to PAF. The substrate is more abnormal in persistent AF (electrical and structural remodelling of the atria) necessitating a more complex ablation strategy, involving focal ablation at sites with fractionated electrograms and the creation of ablation lines. The failure to categorize AF subtype in these studies is likely to inappropriately increase the overall success rate and prevent the actual determinants of long-term success in these distinct populations being reliably identified.

The aim of this study was to identify clinical factors that predict success specifically in patients undergoing ablation for persistent AF.

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Methods

Patient population

Consecutive patients undergoing ablation for persistent AF [AF duration longer than 7 days or requiring cardioversion to restore sinus rhythm (SR)] at our institution between June 2003 and February 2009 were included for analysis. Of the 191,168 (88%) of the patients had long-standing persistent AF (AF duration prior to the ablation procedure of >1 year). Patients awaiting repeat procedures or cardioversions, or who were still within a 3-month blanking period post-ablation were excluded.

Ablation procedure

Patients were treated with warfarin for at least 4 weeks prior to ablation. Warfarin was substituted with weight-adjusted dalteparin (200 IU/kg daily) 3 days prior to the procedure and omitted on the day of the procedure. All anti-arrhythmic medications were stopped at least five half-lives prior to the procedure with the exception of amiodarone. Patients underwent the procedure either under conscious sedation or general anaesthesia. All patients underwent transoesophageal echocardiogram (TOE) immediately prior to ablation to exclude left atrial (LA) thrombus.

A decapolar catheter was placed in the coronary sinus. Long sheaths were used for LA access: Agilis (St Jude Medical, St. Paul, MN, USA), SL0/SL1 (Swartz; St Jude Medical), and Preface (Biosense Webster, Diamond Bar, CA, USA). Transseptal puncture was performed using a BRK or BRK-1 transseptal needle (St Jude Medical). A second sheath was introduced into the left atrium either through the same puncture site or with a second transseptal puncture. Patients were anticoagulated with heparin (100 IU/kg bolus) after LA access followed by further boluses to maintain an activated clotting time >300 s.

We used 3D mapping systems with LA reconstructions to guide ablation (NavX; St Jude Medical or CARTO XP; Biosense Webster). Ablation was performed with 3.5 mm irrigated tip ablation catheters (Therapy Cool Path, Therapy Cool Path Duo; St Jude Medical or Thermocool; Biosense Webster) and a pulmonary vein-mapping catheter (Lasso; Biosense Webster or Optima; St Jude Medical). Radiofrequency ablation in the left atrium was performed at 35 W on the anterior wall, 30 W on the posterior wall, and 20–25 W within the coronary sinus. The tip of the catheter was irrigated with heparinized saline at the rate of 16–30 mL/min.

Contiguous, encircling, ablation lesions were created around ipsilateral pulmonary vein pairs to achieve isolation. Isolation was confirmed during AF by the presence of entrance block using the pulmonary vein-mapping catheter. In addition, linear ablation in the roof or mitral isthmus and ablation of complex fractionated electrograms (CFEs) were performed at the discretion of the operator after pulmonary vein (PV) isolation.

At the end of the procedure, anticoagulation was reversed with protamine 25–50 mg intravenous and venous sheaths removed. Weight-adjusted dalteparin (200 IU/kg daily) was restarted 3–4 h after sheath removal and warfarin re-loaded on the evening of the procedure (1.5× normal dose for 48 h then normal dose). Dalteparin was continued for at least 5 days until the interntional normalized ratio >2.

Post-procedure

All patients were re-started on their previously used anti-arrhythmic treatment with Class IC or III drugs. Anti-arrhythmic treatment was stopped at 3 months in the absence of symptoms, and recurrences within this blanking period were not considered a procedural failure.

Follow-up and monitoring

Follow-up was measured from the last ablation procedure and recorded in months. Patients were monitored with single 12-lead electrocardiograms (ECGs), Holter monitoring for 1–7 days, and pacemaker/implantable cardioverter-defibrillator interrogation (where available) following the 3-month blanking period. Failure was defined as any episode of AF or atrial tachycardia >30 s documented on Holter monitoring or any 12-lead ECG documentation after the blanking period (on or off anti-arrhythmic medication). Where patients had clinical symptoms consistent with AF, efforts were made to document these with Holter monitoring. If symptoms occurred during the monitor period without episodes of arrhythmia, the episodes were not considered recurrences. Success was measured after a single procedure and after up to a maximum four procedures (overall success).

The following factors were included in the statistical model to predict procedural success: hypertension, LA size, ejection fraction (EF), diabetes, prior stroke, or transient ischaemic attack (TIA), duration of persistent AF prior to ablation, hypertrophic cardiomyopathy (HCM), dilated cardiomyopathy (DCM), and coronary artery disease.

Statistical analysis

Clinical characteristics were tested as predictors for AF recurrence using univariate and multivariate survival analysis. Statistical tests were two-sided with an α value <5% considered to be significant. Continuous variables were expressed as mean $\pm$ standard deviation and categorical variables as counts and percentages. Means were compared using Student's *t*-test and categorical values using χ^2 or Fisher's exact test for small groups. Atrial fibrillation free survival was defined as the time following the last ablation procedure.

Survival probabilities were compared using the Cox proportional hazard model for continuous and qualitative data. Multivariate analysis was performed on all variables with a *P* value of <0.2 on univariate analysis using a backwards Wald stepwise method. Estimated mean AF free survival (months) was calculated using the Kaplan–Meier method.

Statistical analysis was performed using SPSS (SPSS Inc., version 17, Chicago, IL, USA).

Results

One hundred and ninety-one patients with mean age 58.2 $\pm$ 12.9 years (79% male) and mean duration of AF 4.0 $\pm$ 3.7 years were included in the analysis. Baseline patient clinical characteristics are shown in *Table 1*.

Ablation procedure

A total of 292 procedures were performed. Mean procedure time was 229 $\pm$ 70 min and screening time 65 $\pm$ 25 min. Wide area circumferential ablation and pulmonary vein isolation were performed in all patients during the first procedure. Isolation was confirmed during AF by the presence of entrance block, using the pulmonary vein-mapping catheter, and in SR demonstrating the absence of local pulmonary vein signals, with pacing manoeuvres if required. In addition, linear ablation in the roof or mitral isthmus and ablation of complex fractionated atrial electrograms were performed at the discretion of the operator after PV isolation. Block was verified in the roof by LA appendage pacing and demonstrating inferior to superior activation pattern in the posterior LA. Block in the mitral isthmus was verified with LA appendage pacing demonstrating proximal to distal coronary sinus

Table 1 Patient characteristics ($n = 191$)

Age (years)	58.2 ± 12.9
Male (%)	151 (79)
Duration of persistent AF (years)	4.0 ± 3.7
Long-standing persistent AF (>1 year duration prior to procedure) (%)	168 (88)
LA size (mm)	47 ± 7
Ejection fraction (%)	57 ± 11
Amiodarone prior to ablation (%)	55 (29)
Number of cardioversions	1.5 ± 1.3
Number of procedures	1.5 ± 0.8
Coronary artery disease (%)	21 (11)
TIA/CVA (%)	18 (9)
Hypertension (%)	69 (36)
Hypertrophic cardiomyopathy (%)	14 (7)
Dilated cardiomyopathy (%)	13 (7)
Diabetes (%)	7 (3.7)

CVA, cerebrovascular accident.
Values are given as count (percent) or mean ± SD.

activation and differential pacing manoeuvres within the coronary sinus timed to the LA appendage. Complex fractionated electrograms were identified by operators to include electrograms with high-frequency activity or highly disorganized activity.

All pulmonary veins were successfully isolated in all cases. During the first procedure, a roof line was created in 136/191 (71%) of patients and a mitral line in 84/191 (44%), and ablation of CFEs in 80/191 (42%).

After ablation, the rhythm was AF in 143/191 (75%) of patients, atrial tachycardia in 25/191 (13%) of patients, and SR in 23/191 (12%). For patients not in SR after ablation, direct current cardioversion was successful in 180/191 (94%).

Complications

Of the 301, 9 (3.0%) patients had evidence of LA thrombus on TOE on admission and did not proceed to ablation. Therefore, 292 procedures were undertaken and of these, 7 procedures were abandoned before LA access was established due to unsuccessful transseptal puncture ($n = 4$), peripheral haematoma ($n = 1$), and pericardial staining after contrast injection ($n = 2$). A further seven patients (2.4%) developed cardiac tamponade during the procedure: five requiring percutaneous drainage and two surgical repair (0.7%). Post-operatively, three patients (1.0%) developed a stroke and two (0.7%) phrenic nerve palsy. Restrictive pericarditis requiring surgical pericardectomy,[8] iatrogenic atrial septal defect with right-to-left shunting requiring percutaneous closure,[9] pulmonary embolus, renal embolus, retroperitoneal bleed requiring blood transfusion, and pseudoaneurysm requiring surgical repair all occurred in one patient each (0.3%). Therefore, the overall major complication rate was 6.2%.

Repeat procedures

One hundred and twenty-four patients (65%) underwent a single procedure, 48 (25%) two procedures, 17 (9%) three procedures, 1 (0.5%) four procedures, and 1 (0.5%) underwent five procedures. The mean number of procedures was 1.5/patient.

Follow-up period

Single procedure success rate was 32% ($n = 191$) after a mean follow-up of 13.5 ± 9.4 months. The overall success rate was 64% after a mean follow-up of 13.0 ± 8.9 months. Of 122, 37 patients (30%) had success defined on the basis of symptoms and single ECG recordings, 78 patients (64%) on extended Holter data (mean 3.2 ± 1.5 days), and 7 patients (6%) from device interrogation. Of patients with successful procedures, 89/128 (70%) were not taking anti-arrhythmic medication.

Predictors of single procedure success

Significant univariate predictor of AF recurrence following a single ablation was LA size [hazard ratio (HR) 1.04/mm with 95% confidential interval (CI) 1.00–1.08; $P = 0.04$]. Atrial fibrillation duration prior to ablation, previous stroke or TIA, HCM, EF, age, gender, coronary artery disease, hypertension, DCM, and diabetes were not (*Table 2*).

Following multivariate analysis, only LA size (HR 1.05/mm with 95% CI 1.02–1.08; $P = 0.001$) was predictive of AF recurrence following a single procedure.

Predictors of overall success

Significant univariate predictor of AF recurrence was LA size (HR 1.08 with 95% CI 1.02–1.14; $P < 0.01$). Ejection fraction, duration of AF, age, gender, presence of HCM, hypertension, diabetes, DCM, and prior stroke or TIA were not predictive of AF recurrence (*Table 2*). Left atrial size (HR 1.07/mm with 95% CI 1.02–1.11; $P < 0.01$) and HCM (HR 2.42 with 95% CI 1.06–5.55; $P = 0.04$) were both multivariate predictors of recurrence after multiple procedures.

Procedural predictors of success

Success after a single procedure was analysed according to the ablation strategy used. With univariate analysis a roof line (HR 0.98 with 95% CI 0.69–1.39; $P = 0.91$), a mitral line (HR 1.21 with 95% CI 0.87–1.68; $P = 0.27$), and targeting of CFEs (HR 0.94 with 95% CI 0.70–1.27; $P = 0.69$) did not predict success after a single procedure. Including LA size in a multivariate model a roof line ($P = 0.28$), a mitral line ($P = 0.29$), and targeting CFEs ($P = 0.40$) were not predictive of success but LA size was (HR 1.06/mm with 95% CI 1.03–1.09; $P < 0.001$).

Left atrial size and procedural success

The relationship between LA dimension and procedural success was analysed with receiver operator characteristics (*Figure 1*). Left atrial size of <43 mm was found to have the highest accuracy for predicting long-term success with a sensitivity of 92%, specificity 52%, positive predictive value of 49%, and negative predictive value of 93%.

Kaplan–Meier AF free survival curves following ablation (LA <43 mm and LA >43 mm) are shown in *Figure 2*. Atrial fibrillation free survival probability was significantly higher in patients with LA<43 mm when compared with patients with LA >43 mm ($P < 0.001$). Estimated 1 year AF free survival was 91% with LA

Table 2 Univariate predictors of success

	Single procedure success			Overall success		
	HR	95% CI	*P*-value	HR	95% CI	*P*-value
Duration of AF	1.07	0.99–1.15	0.11	1.09	0.99–1.21	0.08
LA size	1.04	1.00–1.08	0.04*	1.08	1.02–1.14	0.009*
EF	0.98	0.95–1.01	0.27	0.98	0.94–1.02	0.35
Age	1.00	0.97–1.02	0.81	1.00	0.96–1.04	0.99
Gender	0.57	0.21–1.53	0.26	0.64	0.19–2.18	0.48
CHD	0.75	0.17–3.29	0.71	1.519	0.23–10.12	0.67
TIA/stroke	0.39	0.08–1.90	0.24	0.56	0.06–5.53	0.61
HCM	1.20	0.43–3.39	0.73	2.75	0.79–9.55	0.11
DCM	1.37	0.34–5.54	0.66	2.45	0.25–23.57	0.44
Hypertension	0.86	0.44–1.66	0.65	0.67	0.26–1.70	0.40
Diabetes	2.69	0.73–9.94	0.14	2.55	0.37–17.46	0.34

AF, atrial fibrillation; CHD, coronary heart disease; DCM, dilated cardiomyopathy; EF, ejection fraction; HCM, hypertrophic cardiomyopathy; TIA, transient ischaemic attack.
*Statistically significant.

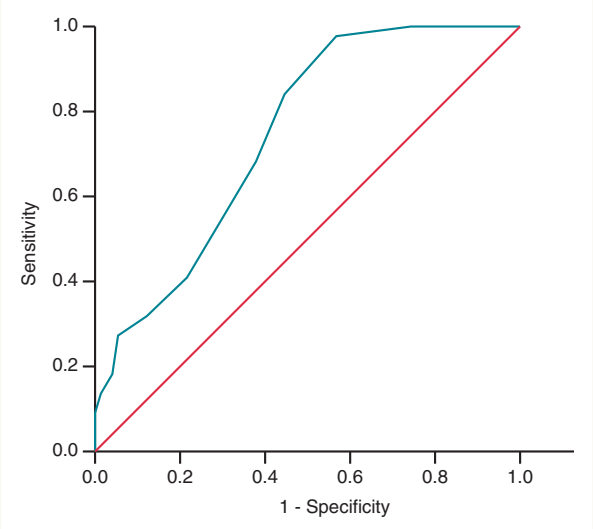

Figure 1 A receiver operator characteristics curve analysis with different left atrial dimensions. An left atrial size of 43 mm had the highest accuracy (sensitivity 92%, specificity 52%) for predicting the overall long-term success. The area under the curve is 0.75 ($P < 0.001$).

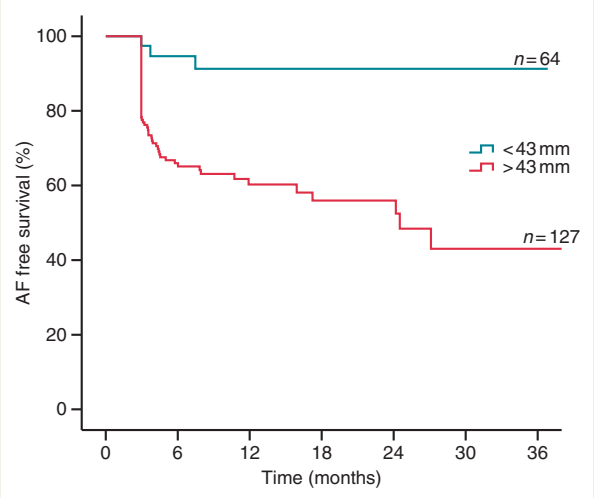

Figure 2 Kaplan–Meier survival estimation for atrial fibrillation (AF) free survival with left atrial size <43 mm and >43 mm. $P < 0.0001$ between groups.

<43 mm and 54% with LA >43 mm. Estimated 2 year AF free survival was 91% with LA <43 mm and 51% with LA >43 mm.

When mean AF free survival is considered against LA size, there is a progressive decrease in survival with increasing the LA size until 46 mm and then no change in survival with increasing the LA size (*Figure 3*).

Left atrial size >43 mm and procedural success

Patients with LA >43 mm were considered as a subgroup for predictors of recurrence after multiple procedures. Left atrial size, gender, age, EF, coronary heart disease (CHD), TIA/stroke, hypertension, diabetes, and DCM were not univariate predictors of recurrence. Hypertrophic cardiomyopathy (HR 3.09 with 95% CI 1.70–7.5; $P < 0.01$) and AF duration (HR 1.07/year with 95% CI 1.00–1.13; $P = 0.03$) were independent predictors of recurrence.

Discussion

Principal study findings

In this population of mainly long-standing persistent AF, LA size is the major determinant for recurrence in ablation for persistent AF following a single ablation procedure and after multiple procedures (HR 1.07/mm with 95% CI 1.02–1.11; $P < 0.01$). Hypertrophic

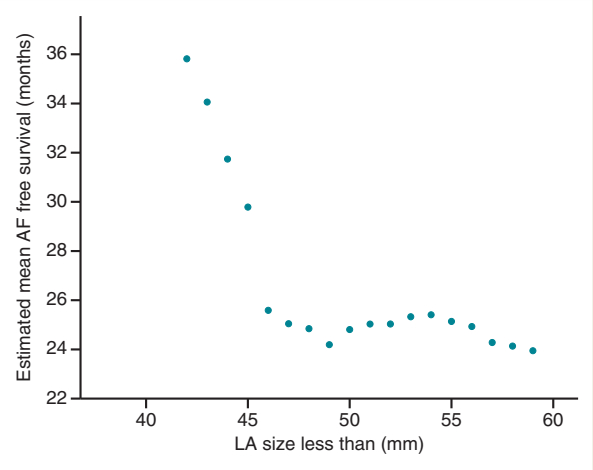

Figure 3 Cumulative estimated atrial fibrillation (AF) free survival (months) for each 2 mm increment in left atrial size including all patient with left atrial size less than the specified value. There is a progressive decrease in atrial fibrillation free survival to <46 mm then there is little effect of increasing left atrial size on atrial fibrillation free survival. Estimated survival not shown for 38–41 mm because there was no recurrence in this group so estimated survival cannot be calculated.

cardiomyopathy is also independently associated with procedural failure (HR 2.42 with 95% CI 1.06–5.55; $P = 0.04$). Estimated AF free survival 2 years following the last ablation is 91% in patients with LA size <43 mm compared with 51% in patients with LA size >43 mm. Left atrial size <43 mm confers a sensitivity of 92%, specificity of 52%, positive predictive value of 49%, and negative predictive value of 93% for predicting freedom from AF. For patients with LA size >43 mm, HCM (HR 3.09 with 95% CI 1.70–7.5; $P < 0.01$) and AF duration (HR 1.07/year with 95% CI 1.00–1.13; $P = 0.03$) were independent predictors of recurrence. With LA size >43 mm, there was no further effect of LA size on the procedural outcome. Type of ablation strategy did not affect procedural success. The data in this study are derived from a cohort with predominantly long-standing persistent AF and dilated atria, which is important when comparing this study with other case series for a number of reasons.

The importance of left atrial size

That LA size is a predictor of success in this population supports the concept of the critical mass hypothesis originally proposed by Moe[10] and recently verified experimentally by Damiano *et al.*[11] Moe hypothesized that a critical mass of atrial tissue is required to support AF caused by multiple wavelets moving randomly throughout the atria. Indeed, these data also replicate the original results of the Cox Maze surgical procedure for the treatment of AF in which success was directly related to LA size.[12] The finding that LA size is an independent predictor of success indicates that despite the complex electrical and structural remodelling processes involved in AF maintenance, a critical mass of viable atrial tissue remains a key determinant in the pathophysiological pathway determining AF persistence.

Left atrial size measured from the parasternal long-axis view using 2D echocardiography has the advantage of being the most universally used measurement of LA size and is, therefore, directly comparable with other studies. However, this measurement has been shown to correlate poorly with LA volume especially in enlarged atria.[13] Measurements that correlate more closely with magnetic resonance imaging-derived LA volumes include reconstructions for 3D echo, LA planimetry either from the apical four-chamber view or biplane estimations combined with an apical two-chamber view.[14] Other measures of LA size may more accurately predict procedural success.

The plateau in the effect on AF survival seen with LA sizes >46 mm has two possible explanations. Left atrial size >46 mm may reflect a critical change in the substrate beyond which ablation becomes less effective. These patients may benefit from different strategies or routine prolonged anti-arrhythmic treatment. An alternative explanation is that LA size measured from the parasternal long axis becomes inaccurate with LA >46 mm. Alternative indices of LA volume may more accurately predict success in these larger atria.

Comparison with previous studies

No studies have previously investigated clinical predictors of ablation success in a population containing only patients with persistent AF. Prior studies included patients with PAF and have, therefore, reported misleading results. Paroxysmal atrial fibrillation is a very different pathophysiological entity requiring a more limited ablation lesion set. As such, it is likely to have different predictors for success.[7,15]

The long-term success of ablation in paroxysmal and persistent AF was recently compared in a large cohort of patients by Bhargava *et al.*[6] (728 PAF vs 676 persistent AF). The overall success rate for persistent AF ablation was 84%. There were several important differences between the paroxysmal and persistent AF groups, including a higher success rate for PAF. In the persistent AF group, longer AF duration predicted failure after a single procedure as did recurrence of AF after a redo procedure. Left atrial size was predictive of single procedure success in PAF but not in persistent AF. This is an unexpected, if not counter-intuitive, finding and is difficult to explain. Patients with persistent AF were divided into two groups: persistent AF (continuous AF for <1 year) and long-standing persistent AF (continuous AF for >1 year). Despite this, patients in the persistent AF group had a mean AF duration of 5.9 years which could not have been continuous for this time period according to their definitions. It is not clear what this discrepancy implies. However, the HRS/EHRA/ECAS Expert Consensus Statement defines the duration of AF as the time patients have spent in continuous AF prior to ablation and this is the definition used in our study.[16] These differences in the definition of AF duration and overall success in the study of Bhargava *et al.*[6] make comparison with our study difficult. Eighty eight per cent of patients in our study had continuous AF duration of >1 year compared with 57% in the study of Bhargava *et al.*,[6] and mean LA size was smaller in that group compared with our equivalent population (47 mm vs. 46 mm, respectively).

Lo *et al.*[17] described the effect of the LA size and procedural AF termination on long-term success in a study of 90 patients with

persistent AF. Left atrial size was greater in patients with long-term failure, in keeping with results from our study, but the overall success rate was higher at 79%. Atrial fibrillation termination did not predict long-term success. Clinical factors were studied in a univariate model to predict AF termination but not long-term success. Success only after a single procedure was reported, and multivariate analysis was not performed. Left atrial size was smaller in the study of Lo *et al.*[17] at 43 ± 8 vs. 47 ± 7 mm in our population, and this may explain why the success rate was higher. The definition of AF duration was also unclear. Only 56% of the study population had 'long-standing persistent AF' despite a reported mean AF duration of 7 ± 5 years. This discrepancy also makes direct comparison with data from this study difficult. It seems likely the median AF duration from the study of Lo *et al.*[17] was low, and therefore, the population is markedly different from our study population.

Berruezo *et al.*[7] reported on a study of 148 patients following AF ablation (90 PAF and 58 persistent AF). Pre-procedural univariate predictors of AF recurrence were age, hypertension, persistent AF, LA size, and left ventricular end-systolic diameter. Left atrial size and hypertension were independent predictors of recurrence. Similar to results from our study, LA size was a predictor of outcome, and yet the mixed population makes interpreting the results difficult. A clear threshold in LA size that predicted success was not identified.

Persistent atrial fibrillation ablation in hypertrophic cardiomyopathy

This study confirms other series which demonstrate a lower long-term success rate in HCM vs. the general AF population. Hypertrophic cardiomyopathy was independently associated with procedural failure (HR 2.42 with 95% CI 1.06–5.55; $P = 0.04$). The substrate in HCM is far more pro-arrhythmic than seen in the typical atria even in PAF patients with mild hypertension or otherwise structurally normal hearts. In the latter, isolation of the PVs has a high chance of maintaining SR long term. This is not the case in HCM where marked structural LA remodelling has already commenced by the time AF develops creating extra-PV drivers and a substrate more likely to independently maintain AF even after ablation of the initial triggers. Di Donnna *et al.*[18] showed that HCM patients with PAF treated with PV isolation and linear ablation had a better outcome than those with persistent AF, who had substantially less success (AF control in 77 vs 50%) reflecting the greater arrhythmogenicity of the HCM substrate even in PAF. Independent predictors of AF recurrence were increased left atrial volume (HR per unit increase 1.009 with 95% CI 1.001–1.018; $P = 0.037$) and New York Heart Association functional class (HR 2.24 with 95% CI 1.16–4.35; $P = 0.016$) in a mixed paroxysmal and persistent AF HCM population. The attrition rate to further AF is significantly higher than the general population as ablation fails to deal with the fundamental pathophysiological changes occurring in the substrate over time with major structural remodelling of the atria in this disease. Longer term studies of defined HCM patient cohorts need to address the efficacy of this approach and which HCM patients are most likely to benefit from AF ablation.

Limitations

Monitoring of patients after the ablation was variable. All patients were followed with 12-lead ECGs and closely questioned about symptoms, but it is recognized that recurrences may have occurred without identification by the investigators and may have been asymptomatic or nocturnal, especially if episodes were of short duration. The majority of patients were followed with Holter monitoring but the timing and the duration of these were also variable.

The technique for ablation was not uniform for the study population. All patients had PV isolation, but the use of linear ablation and CFE ablation was variable; however, comparison of the techniques used showed that they had no influence on single procedure success.

The decision to repeat an ablation procedure is clinician led depending on each case, which may introduce bias into the results for overall success. The single procedure success rate in this study is only 32% and so ablation is a single procedure technique in the minority of patients. It is, therefore, important to consider the patient factors that contribute to overall success, but it is recognized that these results may be subject to bias.

The limitation of the LA size measured from the parasternal long-axis has been discussed, and further studies comparing other indices of LA volumes would be beneficial.

Conclusion

Left atrial size is the major determinant of procedural success in ablation for persistent AF. This should be taken into account when selecting patients for ablation and interpreting the results of clinical trials.

Conflict of interest: none declared.

Funding

This work was supported by funding from the Department of Health's National Institute for Health Research Biomedical Research Centres.

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