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Cryoablation for persistent and longstanding persistent atrial fibrillation: results from a multicentre European registry

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Aims Although cryoballoon pulmonary vein isolation is a well-established treatment for paroxysmal atrial fibrillation (AF), it's role in persistent AF is unclear. We examined procedural success and long-term outcomes of cryoablation in persistent and longstanding persistent AF.

Methods and results International multicentre registry from three UK and eight European centres. Consecutive patients undergoing cryoablation for persistent AF included. Procedural data, complications, and follow-up were prospectively recorded. Patients were followed-up at 3, 6, and 12 months with an electrocardiogram with open access to arrhythmia nurses thereafter. Ambulatory monitoring was dictated by symptoms. Success was defined as freedom from AF or atrial tachycardia lasting >30 s off antiarrhythmic drugs (AADs). Six hundred and nine consecutive cryoablation procedures. Mean procedure and fluoroscopy times were 95 ± 65 and 13 ± 10 min. Single procedure success rates were 368/602 (61%) off AADs over a median of 2.4 (1.0–4.0) years. Arrhythmia-free survival off AADs was 64% and 57% for persistent and longstanding persistent AF at 24 months of follow-up ($P = 0.02$). Rate of repeat ablations was 20% in persistent and 32% in longstanding persistent AF ($P = 0.006$). Cox regression analyses showed a significant association between duration of AF and left atrial diameter and arrhythmia recurrence [hazard ratio (HR) 1.05, *P*-value 0.01 and HR 1.02, *P*-value 0.004].

Conclusion Cryoablation for persistent AF is safe, fast and has good outcomes at long-term follow-up. Cryoablation is reasonable as a first line option for these patients. Short procedure times may help increase capacity of cardiac units to meet the rising demand for AF ablation. Randomised control trials are needed to compare outcomes with different techniques.

Keywords Persistent atrial fibrillation • Cryoablation • Long-term outcomes • Multicentre international registry

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What's new?

- Largest muticentre experience of cryoablation for treatment of persistent and longstanding persistent atrial fibrillation (AF).
- Long-term arrhythmia-free survival off AADs (61% at 24 months) matches that of radiofrequency ablation in this group of patients.
- Short procedure times, day case procedures, and reproducible outcomes despite variable prior experience may help increase capacity for AF ablation.

Introduction

Catheter ablation is an established treatment for symptomatic, drug refractory atrial fibrillation (AF).[1] The cornerstone of AF ablation is pulmonary vein isolation (PVI). Pulmonary vein isolation as an index ablation strategy in persistent AF has demonstrated consistent long-term clinical efficacy outcomes and proven to be equivalent or better than more complex ablation strategies.[2,3]

Conventionally, radiofrequency catheter ablation (RFCA) has been used for PVI. However, this is a technically complex procedure with a long learning curve which restricts this technique to highly specialized centres.[4] In recent years, cryoballoon ablation for PVI has been used as a 'single-shot' approach. The relative simplicity of this technique and short learning curve has potential to improve success rates of AF ablation especially in centres with less experienced operators.[5] Moreover, cryoballoon PVI has been shown to be equivalent to radiofrequency (RF) PVI ablation in patients with paroxysmal AF.[6–8] However, there is very limited evidence for its safety and efficacy in patients with persistent and longstanding persistent AF.[2,9,10] Moreover, it is unclear how or why PVI is effective for these patients and if using the cryoballoon PVI ablation technique would yield similar results to RFCA.

We hypothesized that cryoballoon PVI for persistent and longstanding persistent AF is safe and effective at long-term follow-up. We aimed to assess its safety and efficacy in this international multicentre registry and identify any subgroups of patients who will be poorly served by this ablation strategy.

Methods

Study design

This was a multicentre, registry analyses evaluating the efficacy and safety of cryoballoon ablation for persistent AF. Consecutive patients undergoing cryoablation for persistent AF over 7 years (2011–17) across three UK and eight European centres were included. The present study complies with the Declaration of Helsinki and was approved by the local ethics committee at each centre. Prior to the procedure, all patients gave written informed consent. Although this was a retrospective analysis, all data presented were prospectively recorded in individual ablation registries at all centres. Patient data were de-identified in each individual registry at the respective centres. Anonymized data were collated at Barts Heart Centre. The study was approved by the local clinical effectiveness unit (Institutional Review Board) at an institutional level.

Study patients

All patients undergoing catheter ablation for persistent AF using the cryoballoon were included. Therefore, although patients may have been selected to some extent at each centre on clinical grounds, none were excluded from this analysis. Persistent AF was defined as AF duration greater than 7 days but less than 1 year and longstanding persistent AF was defined as AF duration greater than 1 year as per guidelines.[2]

Catheter ablation procedure

All patients were anticoagulated with either warfarin or direct oral anticoagulant (DOAC) for at least 3 weeks prior to the ablation. For those taking warfarin, the target therapeutic international normalised ratio was 2–3. Procedures were carried out either under intravenous moderate sedation or a general anaesthetic. A transoesophageal echocardiogram (TOE) was not routinely performed prior to all procedures, except in patients who had not been therapeutically anticoagulated for 3 weeks prior to the procedure or were deemed to be exceptionally high risk of stroke (e.g. hypertrophic cardiomyopathy, or previous stroke/transient ischaemic attack (TIA) on anticoagulation). Those with left atrial appendage thrombus did not go on to have an ablation.

Venous access was via the right femoral vein. Two punctures were performed for cryoballoon ablation. After achieving venous access patients were heparinized aiming for an activated clotting time of 300–350 s.

A deflectable sheath (FlexCath Medtronic) was introduced into the left atrium after a single trans-septal puncture. Then the Arctic Front™ (Medtronic) balloon was introduced to the left atrium, inflated and advanced to the ostium of each pulmonary vein and ablation of pulmonary vein antra was performed with at least one application of 180–240 s per vein. The 23- or 28-mm balloon was used according to the anatomy and individual operator preference. Occlusion of each vein was checked with venous angiography. The total number of freezes and duration of individual freeze was at the operator's discretion.

Continuous monitoring of the phrenic nerve during ablation of the pulmonary veins (PVs) was systematically performed by pacing the right phrenic nerve with a quadripolar catheter in the right subclavian or superior vena cava. Refrigerant supply was immediately stopped (double tap technique) if weakening or loss of diaphragmatic movements was noticed. Pulmonary vein isolation (defined as entrance block) was assessed using the Achieve™ (Medtronic) catheter, which allows real time documentation of pulmonary vein signals. Direct current cardioversion was performed at the end of the case if the patient remained in AF. Pulmonary vein isolation was confirmed in sinus rhythm. If PVI was not possible using the cryoballoon, additional RFCA was not performed.

Post-procedure, a transthoracic echocardiogram was performed routinely to look for evidence of pericardial effusion. The oral anticoagulant (whether DOAC or warfarin) was continued following the procedure.

Follow-up

Patients were discharged either the same day or the following day at the operator's/centre's discretion. Routine follow-up was organized as per the standard clinical practice at each centre. Typically, patients were reviewed in outpatient clinics at 3, 6, and 12 months post-index cryoablation procedure. At each follow-up visit, patients were assessed for AF-related symptoms and electrocardiogram (ECG) to document any arrhythmia recurrence. The symptoms were assessed using the European heart rhythm association (EHRA) score, a semiquantitative measure of AF related symptoms and patients' perception of their general health. The EHRA score (EHRA I: no symptoms, EHRA II: mild symptoms, normal daily activities not effected, EHRA III: severe symptoms: normal daily activities effected, EHRA IV: disabling symptoms; normal daily activities

discontinued) was recorded in the electronic AF registry pre- and post-ablation at each follow-up visit. Practice between centres varied, but all centres routinely performed at least one period of ambulatory monitoring within the first year post-ablation. Further periods of monitoring were dictated by symptoms or suspicion of arrhythmia recurrence. All patients had access to arrhythmia nurses. Additional review of medical notes and electronic health records was carried out to ensure capture of all complications and arrhythmia recurrence.

The first 3 months post-AF ablation were designated as a 'blanking period' as per guidelines. A recurrence of arrhythmia during this time was not considered as an efficacy endpoint failure. Patients were allowed to continue antiarrhythmic drugs (AADs) and/or undergo electrical cardioversion during this time at the operator's discretion. However, repeat procedures were not conducted within the blanking period. After the 3-month blanking period, recurrence of arrhythmia was defined as recurrence of AF or atrial tachycardia (≥30 s in duration on ECG monitoring).

Endpoints

Primary efficacy endpoint

The intra-procedural efficacy endpoint was PVI. This was defined as electrical isolation as confirmed by entrance block using the Achieve™ (Medtronic) catheter. Freedom from AF or atrial tachycardia lasting ≥30 s subsequent to the 3-month blanking period after a single procedure and off AADs was defined as the primary efficacy endpoint at follow-up.

Primary safety endpoint

The primary safety endpoint was a composite of major procedural complications including vascular complications (if requiring intervention, delaying hospital discharge, or causing hospital re-attendance), thromboembolic events (TIA, stroke, and/or systemic embolism), phrenic nerve palsy (PNP) persisting after the procedure, cardiac tamponade, procedure-related death, or any other complication that delayed discharge, caused re-attendance to hospital, or required an intervention.

Secondary endpoints

These included procedure and fluoroscopy times, symptomatic improvement as reflected in the EHRA score, rate of repeat ablations, pulmonary vein reconnection rates at repeat procedures, centre variation in outcomes, and factors predicting arrhythmia recurrence post-index ablation (to identify subgroups poorly served by cryoballoon ablation).

Statistical analyses

All data analyses were carried out using SAS version 9.3, statistical software at the primary coordinating centre (Barts Heart Centre, London). For demographic and clinical characteristics, continuous data were presented as mean ± standard deviation or median (range) if not normally distributed. Categorical data were reported as a percentage. Continuous data were compared using unpaired *t*-test (if normally distributed) and Mann–Whitney *U* test if not normally distributed. Categorical data were compared using χ^2 test.

For the primary efficacy endpoint, arrhythmia-free survival analysis was carried out by means of Kaplan–Meier method. The exposure time was calculated as the time from the baseline visit to the last contact (i.e. last follow-up, time of death or documented arrhythmia recurrence time). Cox regression analysis was carried out to assess impact of various clinical factors on arrhythmia recurrence. A *P*-value <0.05 was considered significant.

Table 1 Baseline demographics

***N* = 609**	
Age (years), mean ± SD	63 ± 11
Sex, male, *n* (%)	438 (72)
AF, *n* (%)	
Persistent (<1 year)	487 (80)
Longstanding persistent (>1 year)	122 (20)
First AF episode to ablation (months), mean ± SD	17 ± 20
Background heart disease, *n* (%)	
Normal heart	250 (41)
Ischaemic heart disease	134 (22)
Dilated cardiomyopathy	128 (21)
Hypertrophic cardiomyopathy	12 (02)
Valvular	24 (04)
Others	61 (10)
Hypertension, *n* (%)	329 (54)
Diabetes mellitus, *n* (%)	335 (55)
Previous CVA/TIA, *n* (%)	49 (8)
EHRA classification, *n* (%)	
Class I	6 (1)
Class II	171 (28)
Class III	268 (44)
Class IV	164 (27)
NYHA grade	
Class 1	396 (65)
Class ≥2	213 (35)
CHA_2DS_2VASC score, mean ± SD	2 ± 1.5
Anticoagulation, DOAC, *n* (%)	457 (75)
Antiarrhythmics, *n* (%)	
None	104 (17)
Beta-blocker	158 (26)
Amiodarone	225 (37)
Flecainide	31 (5)
Sotalol	24 (4)
Other	67 (11)
LA diameter (cm), mean ± SD	4.2 ± 1.2

AF, atrial fibrillation; CVA, cerebrovascular accident; DOAC, direct oral anticoagulant; EHRA, European heart rhythm association; LA diameter, left atrial diameter; NYHA, New York Heart Association; SD, standard deviation; TIA, transient ischaemic attack.

Results

Study patients

Six hundred and nine consecutive cryoablation procedures for persistent AF and longstanding persistent AF were performed over 7 years across 11 centres in the UK and Europe. All procedures were performed using the second-generation cryoballoon. Eighty percent of the patients had persistent AF and 20% had longstanding persistent AF. The mean time from the first documented episode of AF to ablation was nearly 1.5 years. Forty-one percent of the study patients had a structurally normal heart. Baseline demographics of the study group are shown in *Table 1*.

Table 2 Procedural characteristics

N = 609	
Elective procedure, *n* (%)	609 (100)
General anaesthetic, *n* (%)	152 (25)
Procedure time (min), mean ± SD	95 ± 65
Fluoroscopy time (min), mean ± SD	13 ± 10
Cryoenergy application time (min), *n* (%)	18 ± 12

SD, standard deviation.

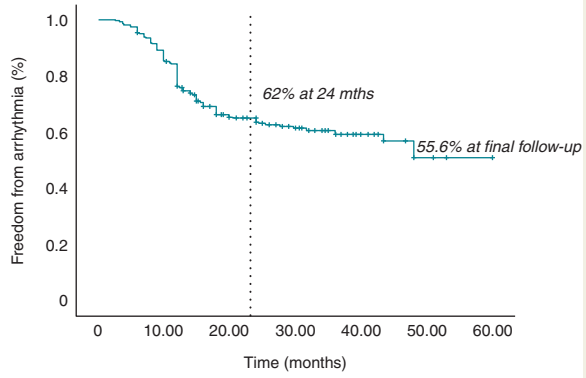

Figure 1 Arrhythmia-free survival on follow-up. Kaplan–Meier curve showing arrhythmia-free survival post-cryoablation for persistent AF. Sixty-two percent patients remained free of arrhythmia at 24 months of follow-up. AF, atrial fibrillation.

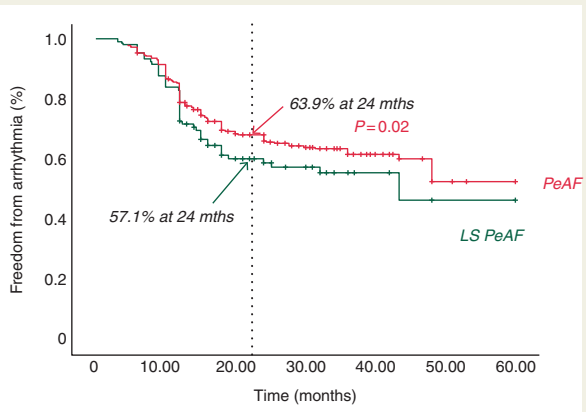

Figure 2 Arrhythmia-free survival—persistent vs. longstanding persistent AF. Kaplan–Meier curve showing arrhythmia-free survival in patients with persistent and longstanding persistent AF. There was a significant difference in arrhythmia-free survival between the groups at 24 months follow-up ($P = 0.02$). AF, atrial fibrillation.

Procedural data

A consultant electrophysiologist was the primary operator for all procedures. All procedures were carried out as per the standard of practice of each centre. About 268/609 (44%) of the cases were performed as a day case. Fifteen percent of the patients were in sinus rhythm and 85% in AF at the start of the case. Cryoablation was performed with patients being in their presenting rhythm. The mean procedure and fluoroscopy times were 95 ± 65 and 13 ± 10 min, respectively. The mean cryoenergy application time was 18 ± 12 min (*Table 2*).

Study endpoints

Primary efficacy endpoint

Acute procedural success (PVI using cryoballoon alone), was achieved in 595 of the 609 patients (98%). Follow-up was available on 602 of the 609 recruited patients (99%) and the median follow-up duration was 2.4 years (interquartile range 1.0–4.0 years). During the follow-up period (subsequent to the 90 day blanking period), 373/602 patients (62%) remained free from AF/atrial tachycardia (AT) and off AADs at 24 months (*Figure 1*). The arrhythmia-free survival rate allowing for AADs was 415/602 patients (69%) at 24 months follow-up. Success in terms of freedom from AF/AT in patients with persistent AF was significantly better than those with longstanding persistent AF with an arrhythmia-free survival rate of 64% vs. 57% at 24 months follow-up ($P = 0.02$) (*Figure 2*).

Of the 14 patients in whom PVI was not achieved using the cryoballoon, no further ablation was performed at the index procedure. For this group specifically, three out of the 14 (21%) remained free from AF/AT and off AADs. The remaining 11/14 patients (79%) had recurrent AF. Repeat ablation procedure was carried out in 10 of these patients wherein the PVs were isolated.

Primary safety endpoint

Twenty-five of the 609 patients (4.1%) sustained an acute and/or peri-procedural complication in this study. These included cardiac tamponade in 4 patients (0.6%), PNP in 19 (3.1%), TIA in 1 (0.2%), and access site haematoma in $n = 1$ (0.2%) (*Figure 3A*). There were no other major bleeding events, peri-procedural strokes, or death. There was no significant centre variation in the safety endpoints.

In the four patients (0.6%) with cardiac tamponade, heparin was reversed in all and pericardial drain inserted. Cardiac surgical intervention was not required in any case. All patients made an uneventful recovery and the mean hospital stay was 2 days. Phrenic nerve palsy (3.1%) was the most frequently observed complication. However, it is noteworthy that the rate of PNPs decreased significantly over the years (13% to 1% of cases per annum over 5 years). *Figure 3B* shows the temporal trend of PNP from 2013 to 2017. A full recovery was observed by 8-month follow-up in all patients as confirmed by fluoroscopic examination. Post-procedural TIA was seen in one patient (0.2%) with no further recurrence or stroke. The patient was on uninterrupted rivaroxaban with no thrombus in left atrial appendage on the pre-procedural TOE. One patient had an access site haematoma. This was managed conservatively and no pseudoaneurysm was identified on vascular imaging. This was listed as a major complication since it delayed discharge.

Secondary endpoints

The mean EHRA score reduced from 3.5 ± 0.5 at baseline to 2.2 ± 1.0 at follow-up ($P < 0.001$). The breakdown of scores pre-ablation is detailed in *Table 1*. It is noteworthy that a proportion of

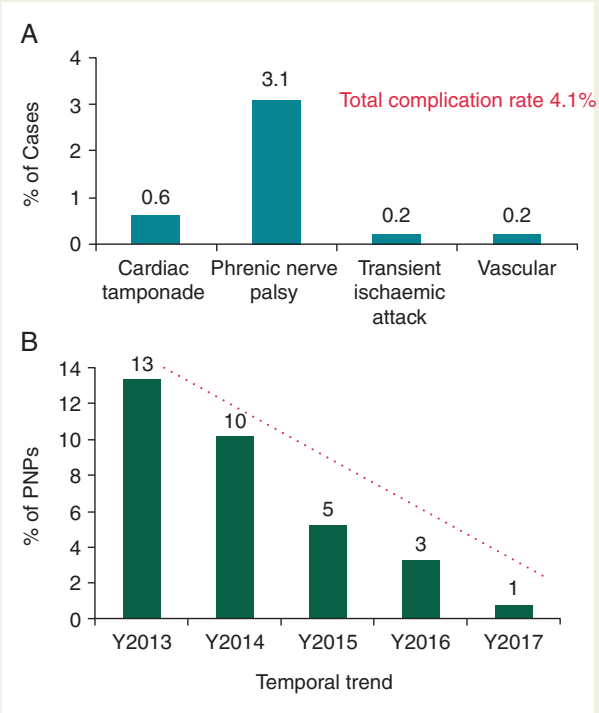

Figure 3 (*A*) Safety endpoint—complication rates and (*B*) PNP—temporal trends. The overall complication rate is shown in (*A*). Twenty-five of the 609 patients (4.1%) reported an acute and/or peri-procedural complication in this study. PNP was the most frequently observed complication. However, the rate of PNPs decreased significantly over the years (13% to 1% over 5 years) (*B*). PNP, phrenic nerve palsy.

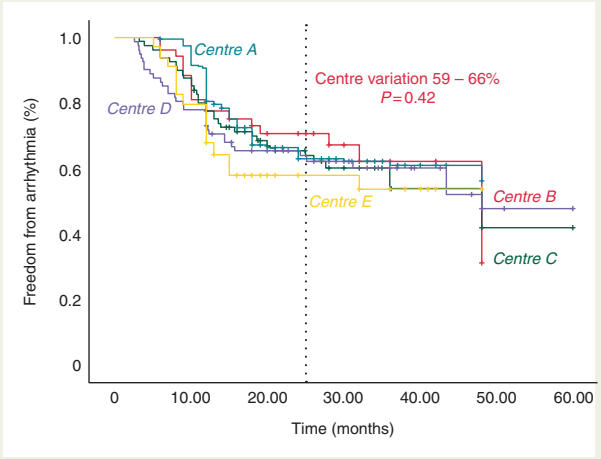

Figure 4 Centre variation in arrhythmia-free survival. Kaplan–Meier curve showing centre variation in arrhythmia-free survival in patients with persistent AF. Three of the eight centres were excluded from the analyses as they had performed less than 30 cases per year. There was no significant centre variation in outcomes with an arrhythmia-free survival rate of 59–66% at 24 months across the low- to high-volume centres ($P = 0.42$). AF, atrial fibrillation.

Table 3 Cox regression analyses for predictors of success

Parameters	Hazard ratio	95% confidence limits	*P*-value
Age	0.98	0.95–1.01	0.34
Gender	1.96	0.83–4.61	0.12
Antiarrhythmics	1.23	0.37–4.08	0.73
Duration of AF	1.05	1.02–1.08	0.01
LA diameter	1.02	1.05–1.21	0.004
Procedure duration	1.01	0.97–1.03	0.19

AF, atrial fibrillation; LA diameter, left atrial diameter.

patients underwent repeat procedures as detailed below and that the symptomatic improvement demonstrated therefore reflects a composite effect of these procedures in some patients.

The arrhythmia-free survival was analysed by centre to assess the impact of different practices/operators on outcomes. Five of the 11 centres were included in this analysis. The remaining six centres were excluded from this analysis as they had performed less than thirty cases in total. We found no significant centre variation in outcomes with an arrhythmia-free survival rate of 59–66% at 24 months across the low- to high-volume centres ($P = 0.42$) (*Figure 4*).

A Cox regression analyses were carried out to assess the impact of different factors on the primary efficacy endpoint. There was a significant association between the duration of persistent AF and left atrial diameter and arrhythmia recurrence post-ablation (HR 1.05 for each increasing month in persistent AF, confidence interval (CI) 1.02–1.08, *P*-value 0.01 and hazard ratio (HR) 1.02 for each increasing millimetre in left atrial diameter, CI 1.05–1.21, *P*-value 0.004) (*Table 3*).

Repeat procedures

Of the 229 (38%) patients who had a recurrence of arrhythmia post-cryoablation, ECG documentation of persistent AF was seen in 65%, paroxysmal AF in 19%, atrial tachycardia in 14%, and typical atrial flutter in 2%. Nearly 60% (134/229) of those with a recurrence underwent a repeat ablation procedure using radiofrequency energy. The rate of repeat ablation procedures was 20% in persistent AF patients and 32% in longstanding persistent AF patients ($P = 0.006$).

Procedural findings at the second ablation were available in all 134 patients. In these patients, one or more of the pulmonary veins had reconnected in a majority, i.e. 95/134 (71%). Right PVs alone were connected in 27%, left PVs alone in 23%, and both in 50%. The number of PVs reconnected at the repeat ablation included zero (29%), one (21%), two (28%), three (12%), and four (10%).

In the 39/134 (29%) patients with all pulmonary veins isolated, additional left atrial ablation included a left atrial roof line in 17/39 patients (44%), mitral isthmus line in 4/39 (10%), posterior wall box lesion in 9/39 (23%), and complex fractionated atrial electrograms in 9/39 (23%). Of this small cohort, 17/39 (43%) patients remained free

of arrhythmia at a mean follow-up of 9.5 ± 7 months; although the majority 30/39 (77%) remained on AADs.

Discussion

In the present study, we report the largest multicentre experience to date of catheter ablation for persistent and longstanding persistent AF using the cryoballoon technology. In over 600 patients who underwent this procedure, this approach was found to be quick at 95 min with almost half of procedures performed as day cases. The safety profile is no different to that reported using the cryoballoon for paroxysmal AF.[7] The intraprocedural efficacy (achieving PVI using cryoballoon alone) was 98%. The arrhythmia-free survival was very similar to that reported for RFCA at 62% at 2 years.

Pulmonary vein isolation for persistent atrial fibrillation

Pulmonary vein isolation is the cornerstone for AF ablation regardless of the energy source or employed technique.[3,6–8] Pulmonary vein isolation has been shown to be non-inferior to more extensive ablation in persistent AF and the role of adjunctive lesions at the time of index procedure is poorly standardized.[11–13] Randomized data using other balloon technologies (the laser balloon) has demonstrated similar outcomes to wide area circumferential ablation using RFCA.[14] Our real-world clinical data is comparable to previously published results using cryoballoon in persistent AF patients. Straube *et al.*[9] reported arrhythmia-free survival of 82% at 12 months and 59% at 18 months; whereas Tondo *et al.*[2] reported an arrhythmia-free survival of 63.9% at 12 months. It is important to note that the arrhythmia-free survival of 62% at 24 months in the present study was in the largest patient cohort yet reported with persistent AF, involved an international multicentre registry, included 20% patients with longstanding persistent AF and had a longer follow-up than previously reported in the literature. Moreover, it is interesting to note that our primary efficacy results were similar to those reported using RFCA or cryoballoon in paroxysmal AF patients in the randomized FIRE and ICE trial.[7]

Factors predicting recurrent arrhythmia

While cryoballoon PVI might be sufficient for some patients with persistent AF, there has been concern that certain subgroups might have a high recurrence rate with this strategy. In our study, we observed a significant difference in arrhythmia-free survival and rate of repeat ablations in patients with persistent AF vs. longstanding persistent AF (64% vs. 57% at 24 months, $P = 0.02$ and 20% vs. 32%, $P = 0.006$). A Cox regression analysis was undertaken to investigate predictors of arrhythmia recurrence and hence identify the subsection of persistent AF patients that might be poorly served by the cryoballoon strategy. We found that duration of persistent AF and left atrial diameter had a significant association with arrhythmia recurrence post-ablation (HR 1.05, CI 1.02–1.08, *P*-value 0.01 and HR 1.02, CI 1.05–1.21, *P*-value 0.004). This is consistent with work by others, and the HR for duration of persistent AF in particular suggests that for each additional month in AF the relative risk of failure rises by 5%. However, the impact of these factors is similar to that reported in studies using RFCA. The cohort with longstanding persistent AF also had outcomes similar to that reported previously for RFCA. There was no clearly identified group with disproportionately poor outcomes compared to that reported for PVI using RFCA previously. Furthermore, although it is possible that patients with more dilated atria and a longer duration of persistent AF might benefit from an ablation strategy beyond PVI, the evidence that this impacts outcomes is currently limited.

Safety of cryoballoon

Although catheter ablation using the cryoballoon is now a well-established technique (especially in paroxysmal AF), it is not free of risk with the major complication rate driven by phrenic nerve damage.[7] The rate of peri-procedural and acute complications in this study was 4.1%. There were no procedural deaths, stroke, or major bleeding events. The rate of cardiac tamponade, vascular complications, and TIA were less than 1% cumulatively, with PNP (3.1%) being the most common safety event in this study. The rate of PNP in our study was lower than the previously reported rates of 13.5% in STOP trial[15] and 10.2% in FIRE and ICE which, like this study, both include patients who underwent ablation some years ago.[7] The rate of PNP decreased significantly over the duration of this study (13% in the first year, reducing to 1% in the 7th and last year of the study). This is likely to be a result of improved operator practice across all centres and is more comparable with contemporary practice reported more recently.[2] Greater operator experience, care to engage the right superior pulmonary vein no deeper than necessary, pacing the phrenic from a more stable position in the subclavian rather than the superior vena cava, and greater use of diaphragmatic electromyography to record compound motor action potentials with phrenic stimulation may all have contributed to this reduction. Phrenic nerve palsy occurring following cryoablation usually recovers, and in fact complete resolution was seen in all 19 patients by 8-month follow-up in this study. These results substantiate the safety profile of cryoballoon ablation, although in a different cohort of patients with persistent and longstanding persistent AF.

Procedural data for cryoballoon pulmonary vein isolation

The mean procedural and fluoroscopy time in our registry were 95 ± 65 and 13 ± 10 min respectively. The procedure times in particular are significantly less than for PVI using RFCA, even in experienced hands and are comparable to what has been reported with cryoballoon ablation by others.[2] Moreover, there was no significant inter-centre variation in primary efficacy and safety outcomes. Although point-by-point RFCA has been the standard of care for AF ablation, balloon base technologies were introduced as a single-shot approach to shorten the learning curve while providing comparable outcomes. The quick procedure times, reproducibility across operators of varied experience, and predictability that we have seen in our study has been reported elsewhere.[5] Cryoablation has been reported to have less operator dependent variability with regards to procedure times, fluoroscopy times and outcomes when compared with patients treated with RF catheter ablation. The short procedure times, day case procedures, and reproducibile outcomes in lower volume

centres using the cryoballoon could help increase the capacity for AF ablation. This could potentially impact on outcomes in healthcare systems with waiting lists by reducing time spent in AF. Randomized control trials are needed to compare cryoablation with different techniques.

Study limitations

Several limitations of this study require consideration.

This is a retrospective, observational and non-randomized study. There are no controls included in this study. The study is reliant on the accuracy of individual prospective ablation registries across all centres to ensure inclusion of all consecutive patients undergoing cryoballoon ablation for persistent AF. There is potential for bias in patient selection and clinical management. However, a large number of patients from an international multicentre study should mitigate this bias. Randomized control trials comparing cryoablation vs. RFCA for persistent AF are required.

Manoeuvres to improve durability of PVI such as waiting periods or adenosine provocation may have influenced outcomes but were not used in this study.

Finally, ambulatory monitoring was not performed consistently post-ablation. This was performed routinely in some centres but was largely symptom guided in others. Hence, arrhythmia recurrence rate and asymptomatic episodes will have been underestimated.

Conclusions

Cryoballoon PVI for persistent and longstanding persistent AF is a safe and effective procedure. The arrhythmia-free survival at long-term follow-up is good and is comparable to that reported for point-by-point RFCA. Increasing left atrial size and time in persistent AF predicted recurrent arrhythmia. Short procedure times, day case procedures, and reproducible outcomes despite variable prior experience may help increase capacity for AF ablation.

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