Cryoballoon ablation for persistent atrial fibrillation: real-life results from a medium-volume centre

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Abstract

Introduction. The value of cryoballoon (CB) ablation for paroxysmal atrial fibrillation (AF) has been well established. However, the safety and efficacy of CB ablation in persistent AF (PerAF) are less well known. The aim of the present study was to assess efficacy of CB in PerAF in comparison to RF ablation and to identify predictors of successful CB ablation in PerAF performed in a medium volume centre.

Methods. Of 303 AF ablations, 92 (30%) procedures were performed in patients with PerAF: 38 CB (mean age 58±9 years, all first-time procedures) and 54 RF ablations, of which in 18 (33%) patients (mean age 57±12 years) this was the first-time procedure. The patients were prospectively followed (mean 14 ± 7 months) by repeated Holter ECG and outpatient visits.

Results. After first-time procedures, recurrences of AF were noted in 15 (40%) patients from the CB group and in 15 (83%) from the RF group ($p < 0.002$). None of the analysed CB procedural parameters predicted the outcome. Of 15 CB patients with recurrences, 5 patients underwent repeated successful RF ablation, resulting in 71% efficacy after two procedures. Of 15 RF patients with an unsuccessful first ablation, 4 had a second successful RF ablation (39% efficacy after 2 procedures) and another 2 had partial improvement (50% efficacy when these patients are included). The remaining patients are waiting for a redo procedure.

Conclusions. CB ablation of PerAF as an initial ablation attempt is safe, relatively effective (60%) and may be successfully performed in a medium volume centre. When recurrences occur, a second RF-based procedure increases the overall success rate to 71%.

Introduction

Ablation for paroxysmal atrial fibrillation (AF) is a well-established technique with a success rate ranging from 60% to over 90%[1]. The main goal of ablation is pulmonary vein isolation (PVI). The results achieved in patients with persistent AF (PerAF) are less encouraging, and reported long-term efficacy of a single procedure is usually not much better than 50%[1]. There are two techniques used for AF ablation. The first one is burning using point-by-point radiofrequency (RF) current delivery and electroanatomical mapping. The second one is freezing by the use of a cryoballoon (CB). While the value of RF ablation in PerAF has been examined by several studies[1] the role of CB ablation in these patients is less clear. A few studies have suggested that this technique may be useful in PerAF, reaching an efficacy rate of 59-65%[2-5]. However, data are limited and come from highvolume and very experienced centres. The safety and efficacy of CB ablation used in patients with PerAF in the real-life setting of smaller centres are not known.

The aim of the present study was to assess efficacy of CB in PerAF in comparison to RF ablation and to identify predictors of successful CB ablation in PerAF performed in a medium volume centre (100-150 AF ablations/year).

Methods

Patients. Between January 2016 and June 2018, 303 AF ablations were performed in our centre. Of these, 92 (30%) procedures were performed in patients with PerAF: 38 CB (mean age 58±9 years, all first-time procedures) and 54 RF ablations, of which in 18 (33%) patients (mean age 57±12 years) this was a first-time procedure. Thus, the final study group consisted of 38 patients treated with CB ablation and 18 patients treated with RF ablation. All demographic, clinical and procedural data were collected prospectively at the time of ablation. The choice of the type of procedure (CB or RF) was left to the discretion of the operator.

Methods

All patients gave written informed consent to undergo AF ablation and to use their medical records for future research.

The CB PVI was conducted in a standard manner. Briefly, after injection of a local anaesthetic, both femoral veins were punctured. One long sheath (8.5 F Swartz, St. Jude, Saint Paul, USA) to cross the interatrial septum was inserted into the right femoral vein. Another two short sheaths were inserted into the left femoral vein for the intracardiac echocardiographic probe (8 or 10 Fr Acunav, Acuson, Siemens, Berlin) and the diagnostic catheter was introduced into the coronary sinus. After crossing the septum and introducing the guidewire into the left superior pulmonary vein (LSPV), the long sheath was replaced with a steerable sheath (14 F., Flexcath, Medtronic, Minneapolis, USA) and a CB (28 mm, second generation) was introduced into the left atrium (LA). Next, the Achieve (20 mm diameter) mapping catheter, (Medtronic, Milwaukee, USA) was placed in the LSPV ostium, the CB inflated and contrast injected to confirm proper occlusion of the LSPV. When PVI was achieved during the first freezing lasting 180–240 s and confirmed by disappearance of PV potentials (PVP) within 60 seconds by recordings from the Achieve catheter, no second cryoapplication was performed. In case of incomplete occlusion, persistence or very late disappearance of PVP, suboptimal temperatures achieved (less than -36°C) or very short thawing time, CB was repositioned and another cryo-application was delivered. Next, CB-PVI of the left inferior pulmonary vein (LIPV), right superior pulmonary vein (RSPV) and right inferior pulmonary vein (RIPV) was performed. Pacing of the right phrenic nerve was performed during CB ablation of the right veins to avoid phrenic nerve palsy. Apart from PVI, no additional ablation (either CB or RF) was performed. If the sinus rhythm did not return during CB ablation, electrical cardioversion was performed and PVI was confirmed. In the case of preserved conduction between the PV and the LA, additional CB was performed in a target vein.

The RF ablation was performed in a standard manner using the 3D electroanatomical system CARTO-3 (Biosense Webster, USA) and a Smarttouch ablation catheter. Two transseptal punctures were performed under intracardiac echocardiography guidance. After reconstruction of the left atrial geometry using merging of the computed tomography or rotational angiography image with the CARTO map, the point-by-point PVI of each vein was performed. The Lasso circular catheter (Biosense Webster, USA) was used to assess PVI and the diagnostic catheter placed in the coronary sinus was used for pacing manoeuvres. After PVI electrical cardioversion was performed if AF persisted and PVI was reconfirmed using the Lasso catheter. In the case of reconnection touch-up RF applications were performed.

No additional lines or ablation of fragmented potentials were performed during the first procedure while during the redo RF ablation these applications were performed if needed, together with PV re-isolation.

Follow-up. All patients were prospectively followed (mean 14 ± 7 months) by repeated 24-hour Holter ECG, usually performed 3, 6 and 12 months after the procedure and examined in the outpatient clinic. Ablation was regarded as successful when the patients had no symptomatic AF recurrences recorded on standard ECG and no AF > 30 s (symptomatic or asymptomatic) was recorded during Holter ECG monitoring.

Statistical analysis

The results are presented as mean±one standard deviation. Continuous variables were compared between the CB and RF groups using Student's t-test and qualitative parameters were compared using the chi square test (with or without Yates' correction) or Fisher's exact test where appropriate. A p value < 0.05 was considered significant.

Results

The comparison of demographic and clinical parameters between the CB and RF groups is presented in Table 1.
The only significant difference was the follow-up duration, which was significantly longer in the RF group.

Table 1. Comparison of demographic, clinical and echocardiographic parameters between the RF and CB groups.

Parameter	RF group n=18	CB group n=38	p
Age (years)	57±12	58±9	NS
Women	5 (27%)	5 (13%)	NS
Duration of AF episode (months)	16±14	10±7	0.027
CHA_2DS_2VASc	2±1.64	1.64±1.15	NS
Follow-up duration (months)	18±8	12±5	0.002
Amiodarone	8 (44%)	15 (39%)	NS
LAA emptying velocity (m/s)	0.45±0.18	0.36±0.16	NS
LVEF (%)	55.9±6.6	55.7±7.8	NS
LA diameter (mm)	41±4.5	47±5.1	NS

Abbreviations: LAA = left atrial appendage; LV EF = left ventricular ejection fraction

After first-time procedures, recurrences of AF were noted in 15 (40%) patients from the CB group and in 15 (83%) from the RF group (p <0.002). None of the analysed parameters (duration of PerAF, CHA2DS2VASc, gender, LA size, left ventricular ejection fraction, LA appendage emptying velocity, number of PV isolated, achieved temperatures, duration of freezes) predicted the outcome (Table 2). Of 15 CB patients with recurrences, 5 patients underwent repeated successful RF ablation, resulting in 71% efficacy after two procedures

Table 2. Comparison of demographic, clinical, echocardiographic and procedural parameters between patients treated effectively and unsuccessfully with cryoballoon technique

Parameter	CB successful n=23	CB unsuccessful n=15	p
Age (years)	57±9	60±10	NS
Women	2 (9%)	3 (20%)	NS
Duration of AF episode (months)	10±7	10±5	NS
CHA_2DS_2VASc	1,52±1,27	1,84±0,89	NS
Follow-up duration (months)	12±5	11±5	NS
Amiodarone	7 (30%)	8 (53%)	NS
LAA empting velocity (m/s)	0,36±0,16	0,34±0,16	NS
LVEF (%)	55±7.5	55±8.7	NS
LA (mm)	46±5	47±5	NS
Number of isolated PV	4	3,9 (all but 1)	NS
LSPV min temperature (^{0}C)	-46,±4,6	-46,7±6,5	NS
LSPV duration of freezes (ms)	249±64	259±115	NS
LIPV min temperature (^{0}C)	-46,5±4,7	-46,4±6	NS
LIPV duration of freeze (ms)	287±125	292±169	NS
RSPV min temperature (^{0}C)	-43,4±4,5	-41,6±5,9	NS
RSPV duration of freeze (ms)	274±117	300±160	NS
RIPV min temperature (^{0}C)	-47,9±5,1	-47,9±5,8	NS
RIPV duration of freeze (ms)	292±118	298±131	NS

Abbreviations: LSPV = left superior pulmonary vein; LIPV = left inferior pulmonary vein; RSPV = right superior pulmonary vein; RIPV = right inferior pulmonary vein. Rest of abbreviations – as in Table 1.

(CB + RF). The remaining 10 patients are waiting for a redo procedure.

Of 15 RF patients with an unsuccessful first ablation, 4 had a second successful RF ablation (39% efficacy after 2 procedures) and another 2 have partial improvement (only paroxysmal AF with minor symptoms) and are not willing to undergo a redo procedure. Thus, the overall clinical efficacy of RF ablation approached 50% when patients with partial improvement were included. The remaining patients are waiting for a redo procedure.

During redo procedures, in each patient at least one PV was re-isolated (most frequently RIPV) and in one patient from the CB group additional roof, anterior and posterior lines were created due to atrial tachycardia. No peri-procedural complications in the CB group were noted, whereas in the RF group there was one pseudoaneurysm.

Discussion

Ablation of PerAF is challenging due to numerous factors involved in arrhythmia mechanisms. Pulmonary veins play a role in initiating and sustaining PerAF, although to a much lesser extent than in patients with paroxysmal AF. In patients with PerAF atrial muscle abnormalities such as fibrosis, scarring and enlargement are the key elements promoting AF[6]. Therefore, simple PVI may not be enough in these patients. Numerous studies have addressed this issue. However, the recent STAR AF II study failed to document the superiority of more complex RF ablation (PVI combined with creating lines or ablating fractionated potentials) over simple PVI[7]. In contrast, another recent study showed that targeting fibrotic and slow conducting areas in the LA increases the success rate[8]. Thus, the optimal method of RF ablation of PerAF remains unknown.

The second technique, CB ablation, has been shown to be equally effective as RF ablation in patients with paroxysmal AF[9]. Again, its value in PerAF is less well documented. Some early studies showed very low success rates in the range of 30-40%, whereas more recent trials reported efficacy exceeding 50%[2-5]. The rationale for using CB in PerAF is based on the fact that CB not only effectively isolates PV but also affects surrounding atrial tissue, and thus also modifies the substrate for AF[10]. Adding posterior wall isolation to PVI increases the success rate of CB in PerAF[10].

The results of our study showed that CB of PerAF as an initial procedure is associated with a reasonable outcome – efficacy of 60%. In addition, if AF recurrences occur, a second ablation using the RF technique is feasible and usually consists of local RF applications at the sites of PV reconnections. In the event of recurrent atrial tachycardia occurring after the first CB ablation, RF also offers a meaningful approach to map and successfully ablate these tachycardias. The cumulative efficacy after CB and RF redo procedures was in our study 71%, which is quite reasonable when compared with RF efficacy, which approached 50% in our cohort. According to the literature, the success of CB may also be improved up to 74% by adding RF applications during the same session for creating lines, fragmented potentials or extrapulmonary triggers[11]. Such an approach, however, significantly increases the cost of the procedure.

The rather low success rate of RF ablation in our patients may increase when all our patients with recurrences undergo a second procedure. Again, we performed only PVI at the first RF procedure and only one patient underwent additional substrate modification during the second procedure, which may be not sufficient in many patients with PerAF. Currently, we perform more extensive second RF ablation and use additional tools such as the ablation index and multipolar recording catheters, which should result in a higher success rate, as shown in the literature[12].

None of the clinical, echocardiographic or procedural parameters predicted efficacy of CB ablation in our patients. This may be due to the small number of patients included in the study. Other studies have shown that such parameters as time to PVI or thawing time may predict the outcome.

The results reported in this paper have been obtained in a medium volume centre, and we believe that they depict the real-life efficacy of ablation in PerAF. According to our results, CB ablation as an initial attempt with the use of RF as a redo procedure in cases of AF recurrence is feasible, reasonably effective and safe. Adding CB-created lines such as a roof line, posterior wall isolation or anterior line will probably increase the efficacy of the procedure. However, we did not perform such an extended procedure during the first ablation session in our patients.

Limitations of the study. Firstly, the study group was small and the duration of the follow-up was relatively short. Secondly, although no specific exclusion criteria were used to select the RF or CB technique, this was not a true prospective, randomised study. Thirdly, longer duration of follow-up in the RF group might have resulted in the higher recurrence rate in these patients compared with the CB group. Fourthly, the follow-up was based on ECG recordings when symptoms occurred and repeated Holter ECG. Thus, we might have missed asymptomatic AF recurrences occurring outside Holter ECG monitoring. Finally, the duration of the AF episode prior to ablation was longer in the RF than in the CB group, which may imply that there were more patients with long-standing PerAF in the RF group in whom ablation efficacy is lower than in PerAF lasting less than one year.

Conclusions. CB of PerAF as an initial ablation attempt is safe, relatively effective (single-procedure success of 60.0%), not inferior to standard RF ablation, and may be successfully performed in a medium volume centre. When after CB recurrences occur, a second RF-based procedure increases the overall success rate to 71%.

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