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Cryoballoon ablation for pulmonary vein isolation in patients with paroxysmal atrial fibrillation

Review of the literature and initial experience

Michael Kühne[a], *Beat Schaer*[a], *Peter Ammann*[b], *Yves Suter*[a], *Stefan Osswald*[a], *Christian Sticherling*[a]

[a] Division of Cardiology, University of Basel Hospital, Basel, Switzerland
[b] Division of Cardiology, Kantonsspital St. Gallen, St. Gallen, Switzerland

Summary

Cryoballoon ablation has emerged as a novel treatment option for drug-refractory atrial fibrillation (AF). The purpose of this manuscript is to report the initial experience of a Swiss centre performing cryoballoon ablation, and to provide a critical review of the literature.

Fourteen patients (age 59 ± 10 years, LVEF 57 ± 5%, left atrial size 41 ± 3 mm) with paroxysmal AF were studied. After transseptal puncture, a 28 mm cryoballoon catheter was inserted into the left atrium. After balloon positioning at the antrum of each pulmonary vein (PV), cryoballoon ablation was performed (5 minutes / application). The endpoint of the ablation was pulmonary vein isolation (PVI).

Eighty-four percent of all PVs could be isolated with the cryoballoon alone. There was no specific distribution of the PVs requiring additional non-balloon ablation. The mean procedure time was 199 ± 56 minutes. One patient developed tamponade requiring drainage. No phrenic nerve palsies occurred. After a period of follow-up of 12 ± 3 months, 10/14 patients (71%) were in sinus rhythm without antiarrhythmic drugs. A review of AF ablation procedures performed at our centre during a one-year period showed that documentation of persistent AF or other arrhythmias were the causes for not using the cryoballoon in 49% of patients because additional linear lesions may be required in these cases.

Cryoballoon ablation is an interesting new tool for PVI. The success rate of 71% after a 1-year follow-up is not higher when compared to radiofrequency ablation. Furthermore, data on long-term outcomes are lacking. Randomised comparisons with radiofrequency catheter ablation are needed.

Key words: cryoballoon ablation; paroxysmal atrial fibrillation; pulmonary vein isolation

Introduction

Atrial fibrillation (AF) is the most common arrhythmia in clinical practice and long-term projections based on epidemiological data predict a two- to threefold increase of the prevalence of the disease by the year 2050 [1, 2]. Over the last ten years, catheter ablation using radiofrequency energy has emerged and evolved tremendously as a new and effective treatment modality for patients with drug-refractory AF [3, 4]. Pulmonary vein isolation (PVI) is the mainstay of any catheter-based treatment for patients with paroxysmal AF. Electrical isolation is commonly performed by a circumferential lesion set around the pulmonary veins. This is achieved in a point-by-point manner and remains challenging and time-consuming. Therefore, the advent of new tools enabling the operator to create a circumferential transmural lesion with a single application of energy has long been awaited by electrophysiologists. One of these tools is a balloon-based catheter ablation system using cryoenergy to create these circumferential

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Abbreviations

AF	atrial fibrillation
AT	atrial tachycardia
CT	computed tomography
IQR	interquartile range
LVEF	left ventricular ejection fraction
MRI	magnetic resonance imaging
PV	pulmonary vein
PVI	pulmonary vein isolation

lesions around the pulmonary veins. Whereas balloon-based ablation systems using high-intensity focused ultrasound (HIFU) or laser were associated with significant safety problems, the feasibility of perfoming PVI using a cryoballoon-based system has been shown in dog models and excised hearts and the first experiences in patients with paroxysmal AF have recently been published [5–14].

The purpose of this paper is to report the initial experience of the first Swiss center to perform cryoballoon ablation using the "single big cryoballoon" technique in patients with paroxysmal AF. Furthermore, the aim is to provide a critical review of the currently available literature, discuss potential advantages and drawbacks of cryoballoon ablation and describe reasons for not using it in unselected patients with AF.

Methods

Design, setting and patient population

This is a prospective observational single centre study. The subjects of the study were 14 consecutive patients with documented paroxysmal AF who were referred to the University Hospital Basel for catheter ablation of AF. All patients had highly symptomatic paroxysmal AF with daily or weekly episodes. Patients with persistent AF, severely depressed left ventricular ejection fraction, significant valvular heart disease, or marked left atrial dilatation (>55 mm), patients with a previous AF ablation, and patients who also had documented arrhythmias other than AF (eg. atrial flutter) were not considered candidates for cryoballoon ablation.

All patients except one underwent magnetic resonance imaging (MRI, n = 4) or computed tomography (CT, n = 9) to assess pulmonary vein anatomy and size. No patient was excluded from the study based on findings on the CT or MRI.

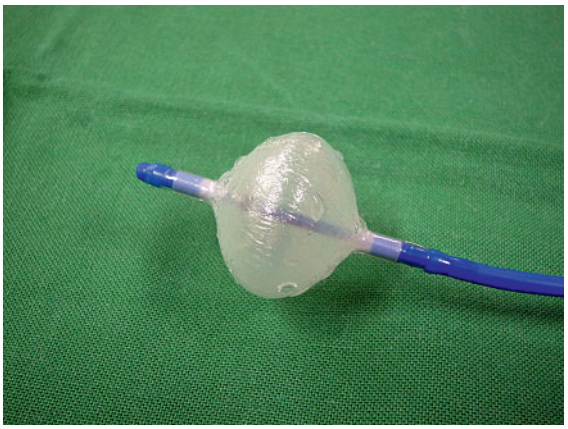

Figure 1

28 mm double lumen cryoballoon ablation catheter (Arctic Front, Cryocath) after inflation in the freeze mode.

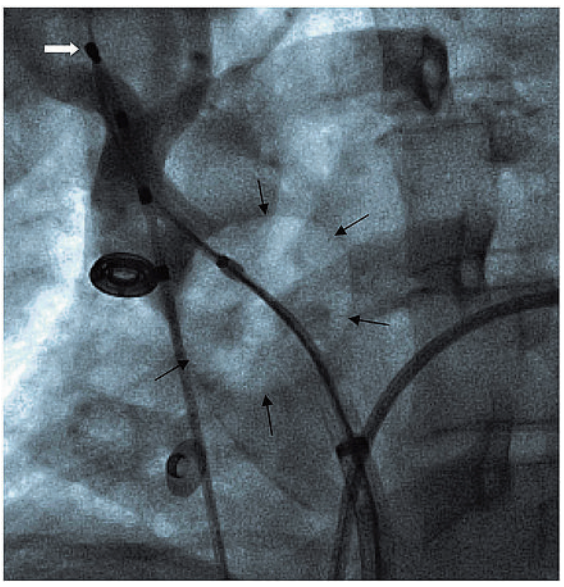

Figure 2

Fluoroscopic image in a left anterior oblique view (43 degrees) showing complete occlusion of the right superior PV (demonstrated by injection of contrast) using a 28 mm cryoballoon catheter (black arrows). The guidewire is advanced into a superior branch of the right superior PV. The quadripolar catheter in the superior vena cava (white arrow) for stimulation of the phrenic nerve is also seen.

Electrophysiological procedure

All patients provided written informed consent before the procedure. All antiarrhythmic drugs except Amiodarone were discontinued 5 half-lives before the procedure. Transoesophageal echocardiography to rule out the presence of an intracardiac thrombus was performed in all patients the day before the procedure.

Blood pressure, oxygen saturation and electrocardiographic monitoring were performed throughout the procedure. The procedures were performed under sedation with a continuous infusion of Propofol as described before [12]. Vascular access was obtained via the femoral veins. A 5F decapolar catheter (Irvine Biomedical Inc., Irvine, CA, USA) was positioned in the coronary sinus as a reference and for atrial pacing. A 5F quadripolar catheter was positioned in the superior vena cava for phrenic nerve stimulation. The intracardiac electrograms and surface electrograms were displayed on an oscilloscope and recorded at a speed of 100 mm/s.

Transseptal punctures using the BRK transseptal needle (St. Jude Medical, Minnetonka, MN, USA) were performed under fluoroscopic guidance using a biplane system. No intracardiac or transoesophageal ultrasound was used. In a left anterior oblique projection, the sheath/dilator/needle unit was pulled down from the superior vena cava until it dropped into the fossa ovalis. After staining the septum with contrast, the needle was advanced into the left atrium. A contrast injection into the left atrium and the measurement of left atrial pressure confirmed the position of the needle whereupon the dilator was advanced into the left atrium. The needle was removed and after inserting a guidewire through the dilator into the left atrium (into a PV), the sheath was advanced into the left atrium.

After transseptal puncture, systemic anticoagulation was achieved using intravenous heparin to maintain an activated clotting time of 300–350 s. A steerable sheath (11.5F, Agilis NxT, St. Jude Medical) for the circumferential mapping catheter (Lasso, Biosense Webster, Diamond Bar, CA, USA) and a second steerable sheath (15F, FlexCath, Cryocath, Quebec, Canada) for the cryoballoon catheter were inserted into the left atrium. Both transseptal sheaths were continuously flushed with heparinised saline at a rate of 50 ml/h.

Cryoballoon ablation

Because PV anatomy was known from MRI or CT, selective PV angiography was not specifically performed at the beginning of the procedure to save contrast medium. As palsy of the right phrenic nerve has been de-

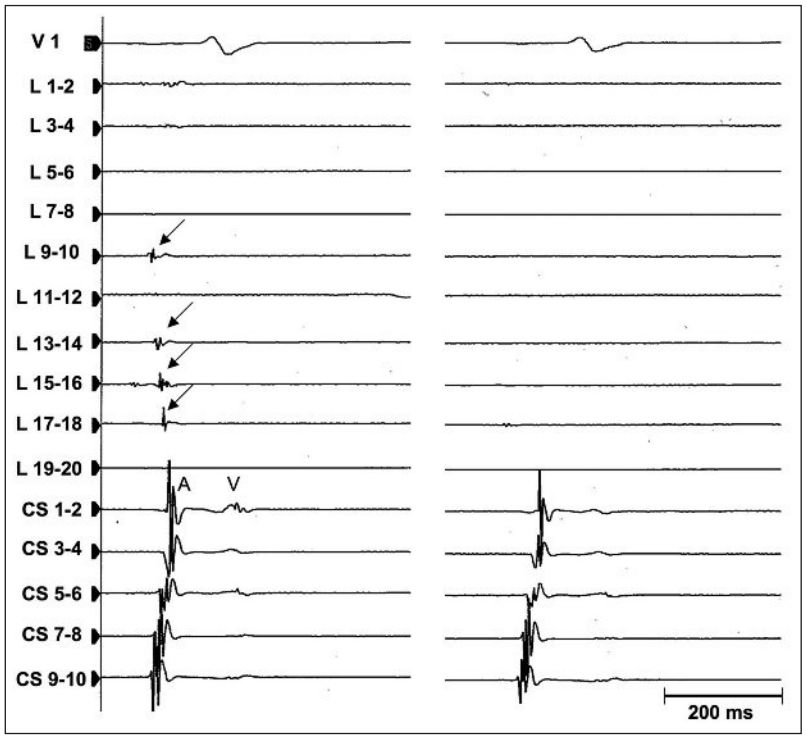

Figure 3

Left panel: Recording of PV potentials in sinus rhythm (arrows) on a circumferential mapping catheter (Lasso) before cryoballoon ablation. Shown are one surface lead (V1), and intracardiac electrograms recording the multipolar ring catheter (L 1-2 (distal) to L 19-20 (proximal) in the right superior PV, and the coronary sinus catheter (CS 1-2 (distal) to CS 9-10 (proximal). The patient was in sinus rhythm and there was conduction into the PV as evidenced by the recordings of PV potentials. A = atrial activation; V = ventricular activation. Right panel: Elimination of all PV potentials on the circumferential mapping catheter after two freezing cycles (2 × 300 seconds) with the cryoballoon catheter.

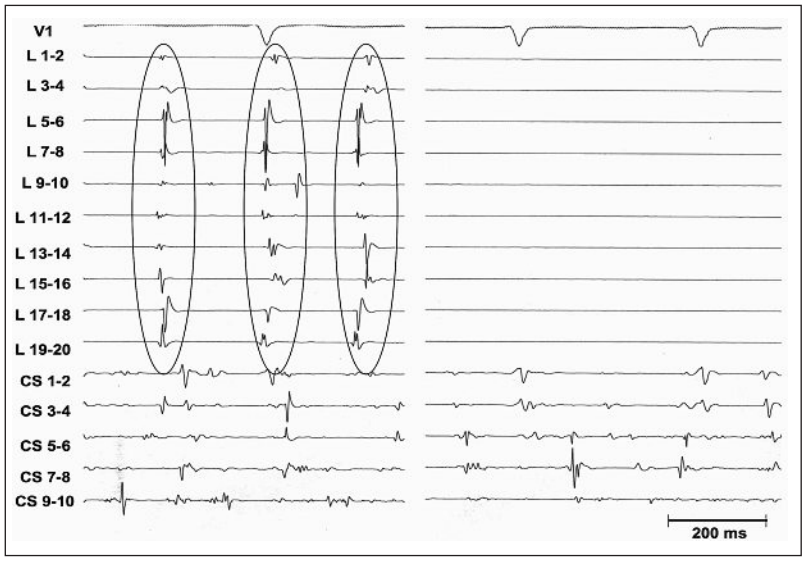

Figure 4

Left panel: Recording of PV potentials (encircled) on a circumferential mapping catheter (Lasso) in a patient with paroxysmal atrial fibrillation. Shown are one surface lead (V1), and intracardiac electrograms recording the multipolar ring catheter (L 1-2 (distal) to L 19-20 (proximal) in the left inferior PV, and the coronary sinus catheter (CS 1-2 (distal) to CS 9-10 (proximal). The patient was in atrial fibrillation during the procedure. There is chaotic atrial activity in the coronary sinus (CS) in atrial fibrillation. Right panel: During a freezing cycle with the cryoballoon at the left superior PV, all PV potentials on the Lasso catheter positioned in the left inferior PV disappeared. This is evidence of electrical interaction of the left superior and left inferior PV (crosstalk technique).

scribed as occurring in a relevant number of patients after ablation at the right superior PV using the smaller (23 mm) cryoballoon, only the cryoballoon with a 28 mm diameter as shown in figure 1 was used [10, 11].

The 28 mm cryoballoon catheter (Arctic Front, Cryocath, 10.5 F shaft) has an inner lumen for insertion of the guidewire and injection of contrast medium to assess occlusion of the PV. Occlusion is indicative of good contact of the balloon with the endocardium, a prerequisite for an effective application of energy (fig. 2). The balloon itself consists of an outer and an inner lumen. During an application of cryoenergy the nitrous oxide (N_2O) refrigerant is delivered into the inner balloon, thereby cooling the inner balloon to a temperature of approximately –80 °C.

Positioning of the balloon was performed using the guidewire in conjunction with the steerable sheath and the deflection of the catheter. Positioning techniques as described by Chun et al. were used [12]. After confirmation of good catheter position by contrast injection (Iopamiro, 1:1 diluted with saline), the freezing cycle with a standard duration of 5 minutes was started. During the freeze, local temperature was continuously monitored from a sensor at the proximal part of the cryoballoon. During ablation of the right-sided PVs, the phrenic nerve was continuously stimulated to assess for phrenic nerve palsy. After two freezes, the circumferential mapping catheter was inserted into the PV to assess for isolation. The endpoint of the ablation was the elimination of all PV potentials (fig. 3 and 4). If ablation using the cryoballoon was not effective in isolating the PV after up to a maximum of six applications, PVI was completed using a conventional cryoablation catheter with an 8 mm tip electrode (Freezor MAX, Cryocath) or an open irrigated-tip catheter with a 3.5 mm tip electrode (Thermocool, Biosense Webster). Needing to switch to a focal catheter was considered a failure in isolating the vein with the balloon catheter.

Postablation management and follow-up

Transthoracic echocardiography was performed in all patients after the procedure to rule out pericardial effusion. Oral anticoagulation was resumed the night of the procedure. Low-molecular-weight heparin (Enoxaparin 1mg/kg subcutaneously every 12 hours) was used until the INR was above 2. Oral anticoagulation was continued for at least 3 months. All antiarrhythmic therapies were stopped after the procedure. Follow-up consisted of outpatient clinic visits at 1, 3, 6, and 12 months after the procedure and included an interview, physical examination, 12-lead ECG, and 24-hour Holter monitoring. A 7-day auto-triggered event monitor was performed at 6 months. Documented episodes of AF (>30 s) and the occurrence of undocumented palpitations (>30 s) were counted as recurrences. The detection of AF was based on RR interval instability (>20%, >10 s). Analysis was performed by two board certified cardiologists. Recurrence rates were analysed with and without the common practice of applying a 3-month blanking period [12]. The occurrence of left atrial tachycardia was also analysed.

Statistical analysis

Continuous variables are presented as mean ± one standard deviation or as median and interquartile range (IQR) in case of skewed distribution. For continuous variables, comparisons were made using Student's *t*-test, or Mann-Whitney *U* test, as appropriate. Discrete variables were compared using Fisher's exact test. A p-value <0.05 was considered to indicate statistical significance. Calculations were made using GraphPad Prism (5.0a).

Results

Patients (table 1)

Fourteen patients (age of 59 ± 10 years) underwent catheter-based ablation of paroxysmal atrial fibrillation using the 28 mm cryoballoon. All patients were refractory to ≥1 antiarrhythmic drugs including Amiodarone in 6 patients. All patients had highly symptomatic AF with >1 episode of palpitations per week, 8 patients had daily symptoms. In all except two patients with coronary artery disease and one patient with a history of myocarditis no structural heart disease was present.

Reasons for not using the cryoballoon catheter

During a one-year period, a total of 105 patients underwent AF ablation at our centre. The cryoballoon catheter was not used in 22 patients because of persistent AF, in 16 patients because of known concomitant cavotricuspid isthmus dependent flutter and 13 patients because of suspected left atrial tachycardia after previous PVI. In these cases, additional linear lesions may be required that cannot be created with the cryoballoon. In total, 49% of patients (51/105) undergoing an AF ablation procedure were not deemed candidates for cryoballoon ablation.

Procedure

Two transseptal punctures were performed in 11 of 14 patients, a single puncture was performed in 2 patients and no transseptal puncture was needed in one patient with a persistent foramen ovale. The procedure time was 199 ± 56 minutes. The fluoroscopy time was 73 ± 30 minutes (dose area product: 37 ± 20 Gy*cm^2).

Pulmonary vein isolation

A total number of 55 pulmonary veins were targeted in 14 patients. Forty-six of 55 (84%) PVs were successfully isolated using the cryoballoon alone. Of the 9 pulmonary veins that were not isolated (in 5 patients) using the cryoballoon alone, 3 were right inferior, 1 was right superior, 3 were left superior and 2 were left inferior PVs. In these 9 PVs, isolation was achieved using an open irrigated-tip catheter (Thermocool, n = 8) or a cryoablation catheter with an 8 mm tip (Freezor MAX, n = 1). The total median time of cryoenergy application was 45 minutes (IQR 40–50). The median freezing time was 10 minutes (IQR 10–15) for the left PVs and for the right inferior PV. The median freezing time for the right superior PV was 10 minutes (IQR 10–10). One patient had a left common PV requiring 20 minutes of cryoenergy for isolation.

Table 1

Patient characteristics (n = 14).

Age (years) – mean ± SD	59 ± 10
Men – n (%)	11 (79)
Duration of AF (months) – median (IQR)	60 (27–135)
Left atrial size (mm) – mean ± SD	41 ± 3
Left ventricular ejection fraction (%) – mean ± SD	57 ± 5
No structural heart disease – n (%)	11 (79)

AF = atrial fibrillation; IQR = interquartile range

Table 2

Procedural details.

	Freezing time (min.)								
Patient #	**LSPV**	**LIPV**	**LCPV**	**RSPV**	**RIPV**	**Total**	**PV isolation (%)**	**Use of special techniques**	**Final PV isolation with**
# 1	10	10		10	10	40	100	none	n/a
# 2	15	15		10	10	50	100	none	n/a
# 3	30	30		20	25	105	25	RIPV: pull-down, hockey stick	RFA
# 4	15	15		10	10	50	100	none	n/a
# 5	10	10		10	15	45	50	none	RFA
# 6	10	10		10	10	40	100	RIPV: pull-down	n/a
# 7	15	10		10	15	50	100	none	n/a
# 8	15	15		15	15	60	50	none	RFA
# 9	10	10		10	10	40	100	RIPV: pull-down	n/a
# 10	10	10		10	15	45	100	RIPV: pull-down; LIPV: hockey stick	n/a
# 11	10	10		10	20	50	75	RIPV: pull-down, hockey stick, big loop	Cryo (FMax)
# 12			20	10	10	40	100	RIPV: pull-down	n/a
# 13	10	10		10	10	40	100	RIPV: pull-down	n/a
# 14	20	5		10	10	45	75	none	RFA
Total	10	10	20	10	10	45	84 ± 25	7/14	5/14

LSPV = left superior pulmonary vein; LIPV = left inferior pulmonary vein; RSPV = right superior pulmonary vein; RIPV = right inferior pulmonary vein; LCPV = left common pulmonary vein; n/a = not applicable; RFA = radiofrequency ablation; Fmax = Freezor Max (conventional cryocatheter)

For 11 of 55 PVs (20%) in 7 patients, special techniques for balloon positioning and ablation as described before were used for PVI (table 2) [12].

Procedural complications

One of 14 patients (patient #2) suffered an acute periprocedural complication with the development of pericardial tamponade after the last freeze at the left superior pulmonary vein. The patient recovered after drainage, but the complication led to a prolongation of the hospital stay.

Three patients experienced postprocedural complications. One patient (#1) had a pseudoaneurysm of the left femoral artery which was successfully treated with compression. Of note, the sheath for the cryoballoon catheter was inserted via the right femoral vein. Another patient (#4) experienced pleuropericarditis requiring treatment with nonsteroidal anti-inflammatory drugs on an outpatient basis. Finally, one patient (#9) suffered from a groin haematoma that was treated conservatively but prolonged hospitalisation for pain management. Of note, no patient experienced phrenic nerve palsy in this series.

Follow-up

With a standard postprocedural blanking period of three months, 10/14 patients (71%) were in sinus rhythm with no documented episodes of AF after a mean follow-up of 12 ± 3 months (without antiarrhythmic drugs). Without a blanking period, 9/14 patients (64%) were in sinus rhythm. When only looking at symptomatic recurrences of AF including undocumented palpitations (>30 s), the success rate was 79%. Of the 4 patients with arrhythmia recurrence, 2 had recurrent AF and underwent repeat left atrial procedures. In these 2 patients electrical reconnection of the PV had occurred in 2/4 and 3/4 PVs, respectively. In the two remaining patients the recurrent arrhythmia was not AF but atrial tachycardia (AT). In one patient, AT could be managed with a class IC antiarrhythmic drug, the other patient was started on Amiodarone and underwent a repeat left atrial procedure showing reconnection of 2/4 PVs. However, AT persisted after isolation of the PVs, and the patient was found to have both cavo-tricuspid isthmus-dependent flutter (typical flutter) and macro-reentrant left-sided AT (mitral isthmus-dependent). He was treated using linear ablation lesions.

Discussion

Main findings

In this study, we describe the initial experience of a Swiss centre performing cryoballoon ablation using the 28 mm cryoballoon in patients with paroxysmal AF. The reported success rate (percentage of patients in stable sinus rhythm without antiarrhythmic drugs) was 71% after a follow-up of 12 ± 3 months. This is a similar success rate when compared to previous studies using one or two cryoballoons with or without the additional use of a conventional catheter and somewhat lower compared to a recent study by Klein et al. who reported a success rate of 86%, however with a shorter follow-up of only 6 months [11–14]. These success rates are similar but not better compared to previous studies in patients with paroxysmal AF undergoing radiofrequency catheter ablation [15, 16]. Outcomes of cryoballoon ablation reported in previous studies are summarised in table 3.

Procedural details

From a procedural point of view, the percentage of PVs that could be isolated using the cryoballoon alone was 84%. The remaining PVs could all be isolated using a conventional ablation catheter. This was equal compared to the study by Van Belle et al., but lower than in the studies by Chun et al. and Klein et al. who were able isolate 98% and 95% of all PVs, respectively [10, 12, 14]. In our series, procedures in which a switch to a conventional ablation catheter was made were significantly longer (244 ± 66 min.) than procedures in which only the 28 mm cryoballoon was used (173 ± 30 min., p = 0.02). Our procedure times (mean

Table 3

Outcomes of cryoballoon ablation in previous studies.

	Patients, n	Left atrial size (mm)	Ablation catheter	PVI using the balloon alone	Follow-up (months)	Success rate
Van Belle et al. [10]	57	43 ± 7	23- and 28 mm and FMax	84%	6	60%
Neumann et al. [11]	346	~41	23- and 28 mm and FMax	78%	12	74%*
Chun et al. [12]	27	42	28 mm	98%	9	70%
Van Belle et al. [13]	141	42 ± 7	23- and 28 mm and FMax	n/a	15 ± 8	59%
Klein et al. [14]	21	38 ± 3	23- and 28 mm and FMax	95%	6	86%

Fmax = Freezor Max (conventional cryocatheter)

* The success rate was 42% in patients with persistent atrial fibrillation who were enrolled in the study (n = 53)

199 ± 56 min.) were similar compared to what large centres have published. Chun et al. reported a median procedure time of 220 minutes using the "single big cryoballoon" technique. They did not require a switch to another ablation catheter in any of their patients in order to achieve a very high PV isolation rate of 98%, which is remarkable. In order to achieve that, they used up to 9 applications of cryoenergy (45 min.) on a single PV, and up to 13 applications (65 min.) in case of the presence of a left common PV [12]. In contrast, we never exceeded more than 6 applications of cryoenergy for treating a single PV. Van Belle et al. reported similar procedure times when using only the balloon (211 ± 108 min.) and also had somewhat longer procedure times when switching to a conventional cryocatheter (261 ± 83 min.) [10]. In the study by Neumann et al., the reported procedure time was 170 minutes (median) [11]. They were able to isolate 97% of all PVs using one or two balloons, or a balloon in combination with a conventional cryocatheter.

Switching to a conventional ablation catheter makes a procedure more complicated and also more expensive. The threshold to switch to a conventional ablation catheter was probably relatively low in our study as we did not use as many attempts of cryoapplications on a single vein as previous studies. It could be argued that special techniques to achieve complete occlusion were not used in 3 patients in whom not all PVs were isolated with the cryoballoon (table 2). However, in these patients, PV anatomy (oval shape of the PV ostium) precluded optimal balloon positioning, and the switch to a conventional catheter was made. It is conceivable that a good occlusion and subsequent isolation of the PV could have been achieved with the use of a smaller cryoballoon. However, because of reports of the occurrence of phrenic nerve palsy especially with the smaller (23 mm) cryoballoon, these smaller balloon catheters were not used in any of our patients. Of note, with the systematic use of phrenic nerve stimulation when performing ablation for the right-sided PVs, none of the patients in our study experienced phrenic nerve palsy.

Performing AF ablation requires procedural skills such as precise manoeuvering of catheters in the left atrium, especially when using large caliber catheters such as the cryoballoon. All procedures were performed by operators experienced in left atrial ablations but no prior experience with balloon-based ablation systems. The number of patients included in this study is probably too small to comment on the learning curve. However, when comparing the procedural details of the 14 patients of our study with 7 additional patients we have treated with cryoballoon ablation in the meantime, the procedure time decreased from 199 ± 56 to 152 ± 18 minutes (p = 0.047), fluoroscopy time decreased from 73 ± 30 to 42 ± 12 minutes (p = 0.007), and the dose area product decreased from 37 ± 20 Gy*cm^2 to 10 ± 6 Gy*cm^2 (p <0.001). In the above-mentioned study by Van Belle et al. the procedure time fell from 375 ± 87 min. to 137 ± 40, and fluoroscopy time from 105 ± 30 to 21 ± 7 min. during the course of the study [10]. However, the number of patients requiring additional energy applications with a conventional catheter remained the same in their study. This implies that a relatively steep learning curve is possible when performing cryoballoon ablation, but that certain limiting factors that may stem from subtle individual anatomical variations remain and on some occasions may prompt the operator to use a second ablation catheter. Exchanging catheters in the left atrium complicates the procedure, may potentially be associated with embolic complications and therefore requires very careful handling of sheaths and catheters. Using an additional catheter obviously also results in additional costs for the procedure, and with budget constraints becoming more important in Switzerland and in most healthcare systems worldwide, this is an important factor to be considered. Cost-effectiveness analyses in this field are still lacking.

Pulmonary vein reconduction and arrhythmia recurrence

In patients with recurrence of AF after PVI using cryoenergy (or radiofrequency energy), reconduction of the PVs is found in up to 100% of patients, on average in 3 PVs [17]. This was also the case in our series where all patients who underwent a repeat procedure had reconduction of 2 to 3 of the 4 PVs. Early reconduction during the first 30–60 minutes after cryoballoon ablation has been reported to be very rare (0–3%) [12, 18]. Based on this, we did not use a specific waiting period to check whether reconduction occurred. However, we did confirm complete isolation of all PVs using a circumferential mapping catheter at the end of the procedure in all patients.

One of the 4 patients with recurrence of arrhythmia in our series developed macroreentrant left-sided AT (mitral isthmus-dependent). This type of arrhythmia appears to be relatively rare when using a cryoballoon-based system for PVI [12]. It may be that this is due to more homogenous ablation lesions compared to lesions created with radiofrequency energy, to more ostial ablation with the balloon as compared to antral PVI using a conventional radiofrequency ablation catheter or to larger conduction gaps. However, recent data from electroanatomical mapping of the left atrium before and after cryoballoon ablation has shown that most PVs undergo antral isolation when performing cryoballoon ablation whereas ostial isolation occurs when the PV is larger than the balloon (i.e. in case of large veins or a small balloon) [19].

Complications

Phrenic nerve palsy (transient or persistent) is very rare with radiofrequency catheter ablation, but is a potential complication associated with cryo-

balloon ablation especially with smaller balloons (23 mm) and larger PVs, and has been reported to occur in up to 10% of cases [10-12]. If an inflated balloon is too far within the right superior PV (not in an antral position), lesion creation may occur at a site very close to the right phrenic nerve. This complication has become less frequent with the use of larger balloon sizes. In our series, we did not have any cases of phrenic nerve palsy using the 28 mm balloon and the systematic use of phrenic nerve stimulation during cryoenergy application at the right-sided PVs.

Groin haematomas may occur with any procedure requiring vascular access, but may be more frequent when sheaths with large calibers are needed. The sheath required for the balloon catheter has a 15 French outer diameter. In our series, we had one patient with a large groin haematoma that could be managed conservatively, but prolonged the hospital stay.

Pericarditis occurs in approximately 1–2% of patients after AF ablation using radiofrequency energy and has not been reported after cryoballoon ablation [20]. In our series, one patient developed pleuropericarditis after ablation requiring treatment with nonsteroidal anti-inflammatory drugs.

PV stenosis was a frequent problem when ablation for PVI was performed within the PV, but has become rare with antral ablation using a conventional ablation catheter. PV stenosis was not found after cryoballoon ablation in previous studies in which patients underwent transoesophageal echocardiography or CT 3 months after the procedure [12, 13].

Potential advantages and drawbacks of cryoballoon ablation

Cell injury due to application of cryothermal energy is complex and related to both the freezing and the thawing process involved. It includes extracellular and intracellular ice formation and vascular injury. Probably due to the pathophysiology of cryothermal injury it appears to prevent the endothelial disruption that is associated with lesions created by radiofrequency energy. This results in less thrombus formation with cryoablation, and this may be important especially in left-sided (left atrial) procedures. However, cryoablation used for ablation of accessory pathways, AV-nodal reentrant tachycardia or typical atrial flutter has been associated with higher recurrence rates compared to radiofrequency ablation. Whether this is also the case for cryoballoon ablation is not known and head-to-head comparisons with radiofrequency ablation are missing in patients with AF [21, 22]. With regard to patient comfort during the procedure, it appears that cryoablation is associated with less pain compared to radiofrequency ablation although some patients report headaches during the freezing cycle, especially with ablation at the left superior PV.

One of the drawbacks of cryoballoon ablation and any balloon-based ablation system is that the tool is not suitable for creating standard ablation lesions (i.e. lines) for treating other arrhythmias such as cavo-tricuspid isthmus-dependent atrial flutter. If one of these arrhythmias occurs in a patient during cryoballoon ablation they cannot be treated with the balloon and a switch to another catheter is required. This has implications with regard to costs. At our centre, persistent AF or the documentation of other arrhythmias in addition to AF before the procedure are the causes for not using the cryoballoon catheter in approximately 50% of patients referred for AF ablation. Another shortcoming of cryoballoon ablation is that real-time recording of PV potentials during the freezing cycle is not possible with the currently available cryoballoon catheter. However, a spiral catheter (Promap, ProRhythm Inc., Ronkonkoma, NY, USA) that was initially designed for the high-intensity focused ultrasound (HIFU) balloon ablation catheter is available and has been used with the cryoballoon (through the inner lumen) for real-time recording of PV potentials during the freezing cycle. However, a recent study showed that successful PVI using the cryoballoon in conjunction with the Promap was only achieved in 54% of all PVs [23]. Therefore, modifications of the spiral catheter are required to use this technique successfully. Finally, another issue with cryoballoon ablation is the fact that a considerable amount of contrast medium is usually used (e.g. 174 ± 50 ml in the study by Chun et al. [12]) making the technique less suitable for patients with renal insufficiency.

Costs

The limitation of price comparisons is that prices may differ significantly between countries and that most hospitals pay individual negotiated prices for individual products. Marketing issues exist and the price of a product may be lower when it is first introduced. The current list price for the Arctic Front cryoballoon catheter in Switzerland is higher than a radiofrequency ablation catheter used for AF ablation. However, comparisons of list prices must be interpreted with caution because additional material such as the console for cryoablation is required for cryoablation and an electroanatomic mapping system may be used for radiofrequency ablation of AF. Preprocedural imaging with CT or MRI is an additional cost factor.

If cryoballoon ablation is performed without the use of additional ablation catheters, without intra- or preprocedural imaging of the left atrium and with shorter procedure times, this new strategy may be cost-effective, but this remains questionable because cost-effectiveness analyses are lacking. Cryoballoon ablation is currently challenged by other novel technologies in the field such as a multi-electrode radiofrequency ablation catheter (Ablation Frontiers Inc., Carlsbad, CA, USA) which allows ablation from several electrodes at the same time and has been shown to result in remarkably short procedure times of <90

minutes [24]. However, a randomised head-to-head comparison with the cryoballoon (and conventional ablation systems) is lacking with regard to costs and also efficacy.

Conclusion

For patients with paroxysmal AF, cryoballoon ablation is an interesting new tool for PVI. In our patients, cryoballoon ablation was associated with a 71% success rate (= freedom from AF) after a 1-year follow-up. This is not higher when compared to radiofrequency catheter ablation, and data on long-term outcomes are lacking. A disadvantage of this ablation technique is that the cryoballoon catheter is not suitable for the creation of linear lesions that may be required in patients with right or left atrial flutter or persistent AF. Randomised head-to-head comparisons with radiofrequency ablation and cost-effectiveness analyses are required.

Correspondence:
Michael Kühne, MD
Division of Cardiology
University Hospital Basel
Petersgraben 4
CH-4031 Basel
Switzerland
E-Mail: kuehnem@uhbs.ch

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