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ORIGINAL ARTICLE

Is radiofrequency energy a necessary and safe complement to cryotherapy for successful pulmonary vein isolation?

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Abstract *Introduction:* Pulmonary vein (PV) isolation is considered the cornerstone of atrial fibrillation (AF) catheter ablation. PV isolation (PVI) by means of cryotherapy has emerged as a promising technique due to both a low thrombogenicity and reduced risk of PV stenosis. The evaluation (need/efficiency/safety) of hybrid therapy (defined as the use of cryotherapy followed by that of radiofrequency energy in a given patient) is the aim of the present study.

Methods: Thirty-four consecutive patients (26 men, mean age: 56.7 ± 9.3 years) with symptomatic drug-refractory paroxysmal AF underwent PVI using a balloon-cryotherapy (BCT). A maximum of four cryotherapy applications was applied per PV and disconnection assessed thereafter using a circular LASSO® catheter. When necessary, PV disconnection was then performed using a 4 mm irrigated-tip catheter. All patients underwent CT-scan evaluation before discharge to detect acute PV stenosis.

Results: PVI could be achieved in all patients. Mean procedure duration was 230 ± 42 min and mean fluoroscopy time was 52 ± 13 min. Hybrid therapy was needed to achieve PVI in 26 of 34 (76%). With cryoablation solely, PVI was achieved in 90 of 136 (66%) targeted veins, efficacy being

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higher in superior as compared to inferior PVs (87% vs. 46%, $p < 0.001$). Besides one patient with permanent right phrenic nerve injury, no other procedure-related complications were observed. After a mean follow-up period of 8 ± 3 months, 28 patients (82%) did not experience AF recurrence (including six patients on antiarrhythmic drugs).

Conclusions: Our study suggests that hybrid ablation therapy is necessary in most patients to achieve PV disconnection after a maximum of four blinded applications of balloon-cryotherapy (especially in inferior PVs), with a significant short-term success rate.

1. Introduction

Focal ablation of triggers within the PV was described as a curative tool for AF treatment[1] to be modified later to segmental or antral PV ablation.[2] Different ablation strategies and techniques have been developed to achieve efficient PV electric isolation (PVI). Cryotherapy evolved as an effective and safe catheter ablation tool for treating various arrhythmic substrates.[3,4] The introduction of BCT has allowed antral PV electric isolation, however anatomical and technical challenges may contribute to relatively long procedure and fluoroscopic exposure times using it as a sole ablation tool.[5] The evaluation (need/efficiency/safety) of hybrid therapy (defined as the use of BCT followed by that of radiofrequency energy in a given patient) is the aim of the present study.

2. Methods

2.1. Patients' characteristics

The study population consists of 34 consecutive patients (26 men, mean age: 56.7 ± 9.3 years) with symptomatic drug-refractory paroxysmal AF of 5.3 ± 3.5 years duration. A mean of 3 ± 0.7 antiarrhythmic drugs had failed to control AF prior to the ablation procedure. Two patients had hypertensive cardiomyopathy, two had coronary artery disease, one had hypertrophic cardiomyopathy, one had mild rheumatic mitral stenosis, one had aortic valve prosthesis and 23 had no evidence of structural heart disease.

2.2. Patients' preparation

Left atrial anatomy was assessed 1 day preceding the electrophysiological study as all patients underwent an ECG-gated helical multislice CT scan of the chest. Images were acquired using a 64 row multidetector CT scanner (GE Light-Speed®, GE Healthcare), where the LA volume, the number, size and shape of the PV could be assessed. PV shape was assessed by calculating the PV index as described previously.[6] All patients provided a written informed consent. Oral anticoagulants were replaced on admission by intravenous heparin to maintain a partial-thromboplastin time of 60–90 s (control, 30 s), and a transesophageal echocardiogram was performed before each procedure to exclude LA thrombus.

2.3. Electrophysilogic procedure and ablation

Through a right femoral venous approach, a 5F quadripolar catheter (XTREM®, ELA Medical, Sorin Group) was advanced in the distal coronary sinus. Left atrium was accessed through a transseptal puncture using an 8F long sheath (SL1®, St. Jude Medical), to be replaced over a guide wire by a 12F transseptal sheath (FlexCath®, Cryocath). Subsequently, intravenous heparin was administered at a dose of 0.5 mg/kg, followed by a repeat bolus to ensure an antithrombin coagulation time constantly >250 s. Sedation was obtained with 10 mg nalbuphine intravenous with incremental doses of 5 mg as necessary throughout the procedure.

A circular mapping catheter (LASSO®, Biosense-Webster) introduced through the transseptal sheath was placed on the PVs ostia (defined by PVs angiography) to record PV potentials prior to PV ablation (Fig. 1). Bipolar electrograms (band pass, 30–500 Hz) were recorded on a multichannel polygraph (LabSystem PRO®, Bard Electrophysiology).

The circular mapping catheter was replaced by a 12F balloon catheter. One of two available balloon sizes (23 or 28 mm) was chosen with respect to the PV ostial dimensions on the CT scan images. The balloon catheter was inflated in the left atrium and advanced to occlude the ostium of each PV. Depending on the quality of PV occlusions assessed by PV angiograms (Fig. 1), a minimum of two average or good occlusions should be achieved per PV and within a maximum of four applications (5 min per application). Occlusion of the PV were classified as good (no contrast leakage), average (leakage of contrast from one of the four quadrants of each PV; anterior, posterior, inferior and superior quadrants), and bad (leakage of contrast from more than one quadrant of the PV ostia). The quadripolar catheter was placed in the superior vena cava for phrenic nerve pacing during BCT application for the right PVs. If any loss of capture was detected, BCT was terminated immediately (Fig. 2).

The balloon catheter was replaced by the circular Lasso® catheter to check for PV electric isolation (Fig. 1).

If electric isolation of any of the targeted PV was not achieved by the BCT solely, hybrid radiofrequency ablation was applied as a 4 mm irrigated-tip catheter was introduced to the left atrium targeting the PV electric potentials on the Lasso® catheter. Radiofrequency energy was delivered to PV-atrial electric connections with a power of 25–30 W using irrigation rates of 5–60 ml/min (0.9% saline via a Cool Flow pump; Biosense-Webster) to achieve the desired power delivery. RF energy applications were discontinued when the local PV electrograms were abolished on the circular mapping catheter.

2.4. Post ablation management

A control transthoracic echocardiogram was performed within 2 h after ablation and the day after. A control chest CT-scan was performed on the day after ablation to detect early PV stenosis. Oral anticoagulants were reinitiated the day after ablation and maintained for at least 6 weeks. Heparin administration was

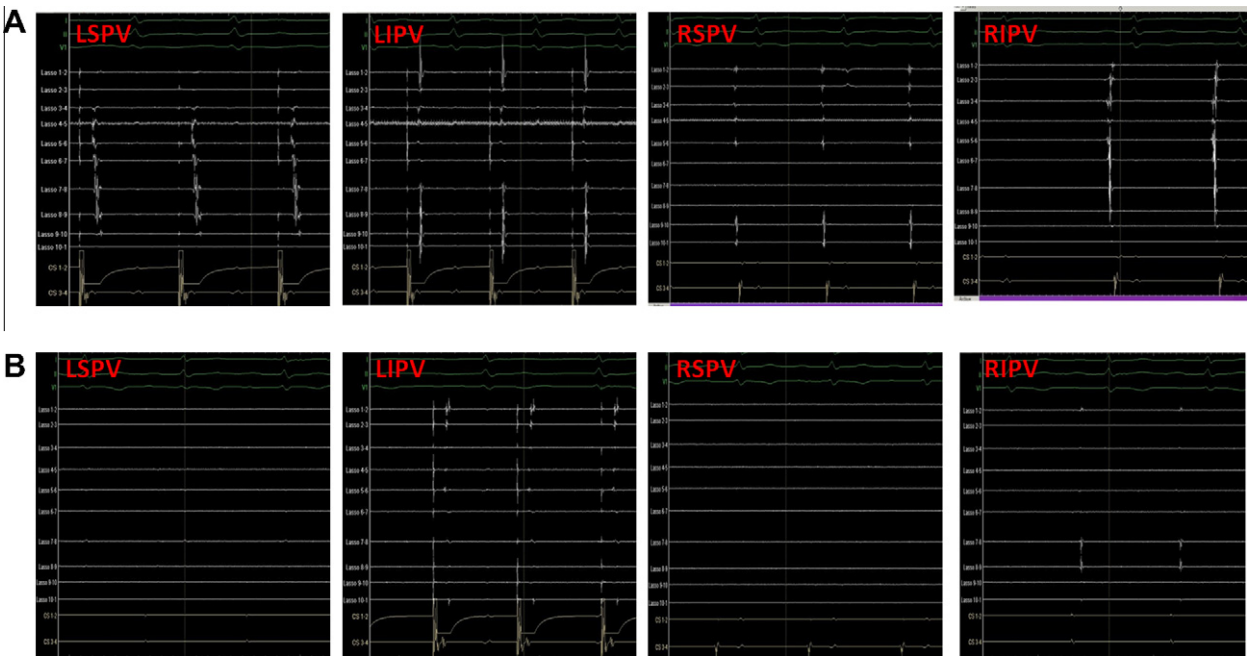

Figure 1 Intracardiac tracings of the PV potentials detected on the Lasso catheter placed at the 4 PV ostia before cryo application (A) and following cryo application (B). Note the residual PV potentials in both LIPV & RIPV denoting incomplete PV isolation. LSPV: left superior pulmonary vein, LIPV: left inferior pulmonary vein, RSPV: right superior pulmonary vein & RIPV: right inferior pulmonary vein.

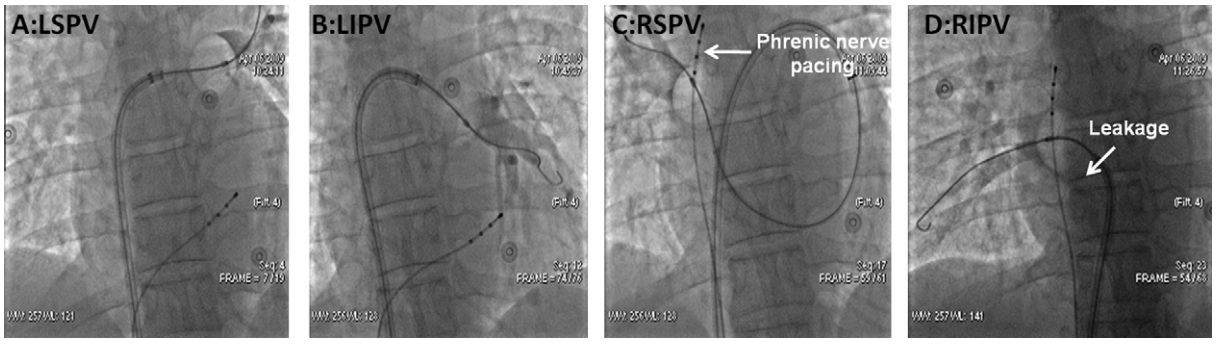

Figure 2 An example showing the balloon accluding the 4 PV with verification of occlusion using contrast injection. Note the proper occlusion of all the PV (A–C) except the RIPV that shows contrast lealage at its inferior border shown by the white arrow (D). A quadripolar catheter is placed in the SVC for phrenic nerve pacing during cryo ablation of the RSPV (C). LSPV: left superior pulmonary vein, LIPV: left inferior pulmonary vein, RSPV: right superior pulmonary vein & RIPV: right inferior pulmonary vein.

maintained (intravenously for 24 h then subcutaneously) for 3 days after the international normalized was >2.

Patients were monitored by telemetry for at least 3 days after ablation, then discharged and followed on an out-patient basis with clinical evaluation and 24-h Holter recordings performed regularly. All antiarrhythmic drugs were discontinued following the procedure unless AF recurrence was detected during follow up.

3. Results

A total of 34 patients were enrolled in the study. Total mean procedure duration was 230 ± 42 min and a mean fluoroscopic exposure time was 52 ± 13 min. When using the 23 mm cryoballoon, the total procedure time was insignificantly shorter (219 ± 36 min) compared to the 28 mm cryoballon (241 ± 44 min). Total fluoroscopic exposure time was the same for both balloons (44 ± 13 vs. 44 ± 14 min for the 23 and 28 mm balloons, respectively).

As measured on the CT scan images, mean LA volume was 111 ± 23 ml, a total of 136 PV were identified to be targeted for ablation and isolation. BCT alone was not sufficient to achieve isolation of all the PV in 26 patients (76% of patients) where hybrid radiofrequency therapy was needed to achieve complete PVI.

3.1. PVI using BCT alone

Isolation of PV was achieved in 90 of 136 (66%) targeted veins using BCT alone with the highest efficacy in the superior PVs compared to the inferior PVs (87% vs. 46%, $p < 0.001$).

Electric isolation using BCT alone was observed in 88% of LSPV (30/34), 85% of RSPV (29/34), 64% of LIPV (22/34) and 26% of RIPV (9/34).

Pulmonary vein index was the predictor of successful PVI using BCT alone for the left PVs. whereas for the right PVs, no clinical or anatomical factors were identified as predictors of successful PVI (Table 1).

Table 1 Pulmonary vein index for isolated and non-isolated PV.

	LSPV	LIPV	RSPV	RIPV
Isolated PV index	1.2 (1.1–1.5)	1.2 (1–1.7)	1.1 (1–1.7)	1.1(1–1.2)
Non-isolated PV index	1.7 (1.6–1.7)	1.5 (1–1.5)	1.1 (1.1–1.7)	1.2 (1–1.4)
P-value	<0.05	<0.05	NS	NS

Table 2 Minimum temperature achieved during cryotherapy in isolated and non-isolated PV.

	LSPV	LIPV	RSPV	RIPV
Minimum temperature in isolated PV	-55 ± 10 °C	-54 ± 10 °C	-58 ± 9 °C	-51 ± 8 °C
Minimum temperature in non-isolated PV	-40 ± 6 °C	-41 ± 5 °C	-48 ± 5 °C	-39 ± 5 °C
P-value	<0.05	<0.05	<0.05	<0.05

The mean temperature achieved during cryotherapy was significantly lower in all isolated PV compared to non-isolated ones (Table 2).

3.2. PVI using hybrid therapy in comparison to BCT alone

Following BCT, radiofrequency energy was needed to achieve complete isolation in 46 PV. The mean RF duration applied was 2.8 ± 1.3 min with the highest duration at the RIPV and the lowest at the RSPV (Table 3).

Table 3 Duration of hybrid RF energy applied to achieve complete PVI.

	LSPV	LIPV	RSPV	RIPV
Mean RF duration (min)	1.9 ± 0.9	2.8 ± 1	1.2 ± 0.5	3.3 ± 1.2

Table 4 AF recurrence during follow up.

	AF recurrence with antiarrhythmics	AF recurrence without antiarrhythmics
All patients ($n = 34$)	12/34 (35%)	6/34 (16%)
BCT alone ($n = 16$)	5/16 (31%)	1/16 (6%)
Hybrid therapy ($n = 28$)	7/28 (25%)	5/28 (18%)
P value	NS	<0.05

4. Complications

Besides one patient with permanent right phrenic nerve injury, no other procedure-related complications were observed.

4.1. Recurrence rate

After a mean follow-up period of 8 ± 3 months, 28 patients (82%) did not experience AF recurrence (including six patients on antiarrhythmic drugs. AF recurrence rate was significantly higher in patients using hybrid therapy (18%) compared to BCT alone (6%) (Table 4).

5. Discussion

Successful PVI remains a cornerstone in the ablative therapy of atrial fibrillation.[1] Cryo energy ablation of the PV using a balloon has been described as a therapeutic approach for circumferential PV ablation.[5] Long procedure time, fluoroscopic exposure and the ability to isolate all PV remained as technical challenges for BCT procedures.[7]

In our study, we evaluated the utilisation of BCT for AF ablation. In addition we studied the feasibility and efficacy of hybrid RF ablation as a complement to BCT.

In this study, 66% of the PV were successfully isolated with BCT alone which is slightly lower than the 84% and the 98% achieved by Van Belle et al.[7] and Chun et al.[5] This could be explained by the fact that our cryo applications were limited to a maximum of four before shifting to hybrid RF therapy.

In agreement with other studies,[5] the RIPV was the most challenging to achieve isolation using BCT. It was the only PV that could not be isolated in the single big cryoballoon study by the Hamburg group.[5] This could be attributed to anatomical challenges to rotate the whole transseptal sheath and the balloon to occlude the RIPV due to the small endoluminal distance between the fossa ovalis and the RIPV.[8]

It has been proven in our study that the anatomical shape of the PV ostia is a major determinant to achieve acute PVI using BCT for most of the PV. The PV index which is an indicator of the PV ostium shape was directly related to successful PV isolation with BCT.

Achieving lower balloon temperature was associated with successful PVI using BCT which could be attributed to better occlusion and contact at the PV. This has been proved recently by the Hamburg group.[7]

It has been proved in animal models that delivering RF and cryoenergy, simultaneously and sequentially was as effective as delivering any of them independently.[9] However in our study, patients with hybrid therapy had a higher recurrence rate compared to BCT alone during the follow up period. This finding may raise the question on the effect of RF energy following cryoenergy on the long term lesion evolution.

6. Conclusion

Our study suggests that hybrid ablation therapy is necessary in most patients to achieve PV disconnection after a maximum of four blinded applications of balloon-cryotherapy. Radiofrequency energy following cryoenergy may be responsible for higher recurrence rates post ablation.

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