



Long-term healthcare utilization, symptom burden, and quality of life after cryoballoon ablation in Korean patients with atrial fibrillation

Real-world experience from the Cryo Global Registry



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Korean Heart Rhythm Society

COI Disclosure

Houng-beom Ahn

The authors have no financial conflicts of interest
to disclose concerning the presentation



Study Overview – Cryo Global Registry

Design of Cryo Global Registry (NCT02752737):

- Prospective, global, multi-center, observational post-market real-world registry
- Subjects followed to align with standard-of-care, with required annual visit until study exit (up to 24 months)

Purpose:

Global clinical performance & safety evaluation in patients with atrial fibrillation treated by CBA.

Study Start Date: May 2016

Estimated Primary Completion Date: December 2022

Estimated Study Completion Date: December 2024



Study Overview – Korean Cohort

12-Month outcome published: Lim HE, Oh IY, Kueffer FJ, van Bragt KA, On YK. Korean Circ J. 2022;52:755-767. doi: 10.4070/kcj.2022.0127

Background

Atrial fibrillation (AF) is the most common atrial arrhythmia and is an increasing healthcare burden in Korea. Cryoballoon ablation (CBA) is a well-established treatment for the alleviation of AF symptoms.

Korean cohort sub-analysis:

- 299 patients enrolled in 3 Korean centers between Apr 2019 to May 2020.
- 24-months follow-up per the hospitals' standard of care.

Purpose of sub-analysis:

This sub-analysis of the Cryo Global Registry aims to describe **longer-term healthcare utilization, quality of life, and symptom burden** in Korean patients with AF treated by CBA (Arctic Front™ Family of Cardiac Cryoablation Catheters).

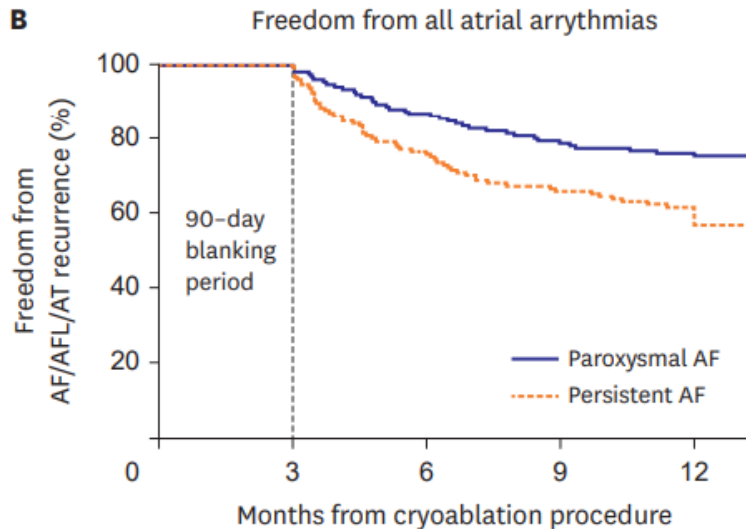
Principal Investigator Name	Site Name	Enrolled Subjects
Hong Euy Lim	Hallym University Sacred Heart Hospital	100
Young Keun On	Samsung Medical Center	100
Il-Young Oh	Seoul National University Bundang Hospital	99
	Total	299



Cryoballoon Catheter Ablation in Korean Patients With Paroxysmal and Persistent AF: One Year Outcome From the Cryo Global Registry

Freedom from AF/AFL/AT at 12 months:

- Paroxysmal AF: 75.2% (95% CI: 67.4-81.3%)
- All Persistent AF: 56.7% (95% CI: 48.2-64.4%)

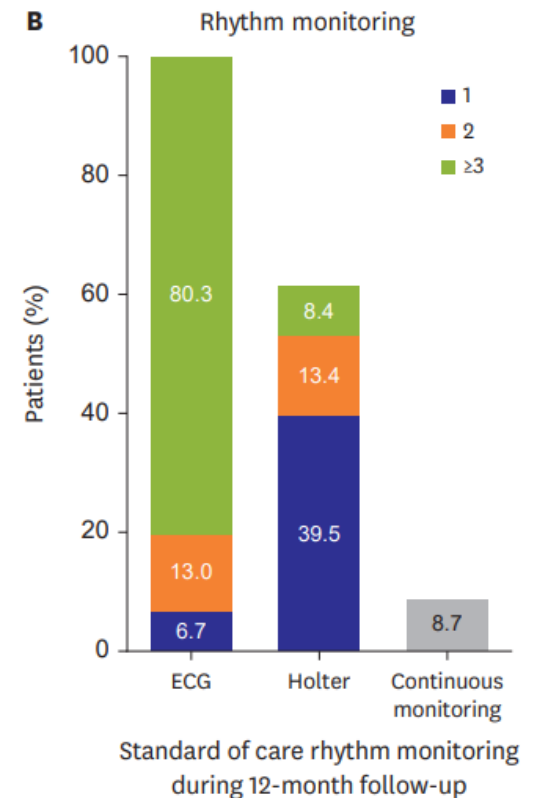


Numbers at risk

Paroxysmal AF	151	149	129	118	113
Persistent AF	148	144	109	95	88

Rhythm Monitoring:

- Average number of clinical visits was 4.7 ± 1.1 times
- All subjects received a 12-lead ECG
- Holter monitoring was used at least once in 61% of subjects



Korea Cohort Subject Characteristics

Baseline Subject Characteristics (N=299)	
Age (years; mean \pm SD)	60 \pm 11
Female Sex (N (%))	74 (24.7%)
Diagnosed with Atrial Fibrillation (years; mean \pm SD)	2.8 \pm 3.0
Paroxysmal Atrial Fibrillation (\leq 7 days; N (%))	150 (50.2%)
All Persistent Atrial Fibrillation ($>$ 7 days; N (%))	149 (49.8%)
Number of Failed Antiarrhythmic Drugs (mean \pm SD)	1.2 \pm 0.6
0 Previously Failed AADs (N (%))	13 (4.3%)
- On AAD at Baseline	9 (3.0%)
- Not on AAD at Baseline	4 (1.3%)
Body Mass Index (kg/m ² ; mean \pm SD)	25 \pm 3
Left Ventricular Ejection Fraction (%; mean \pm SD)	59 \pm 8
Left Atrial Diameter (mm; mean \pm SD)	43 \pm 7
CHA ₂ DS ₂ -VASc Score (mean \pm SD)	1.8 \pm 1.4
Diabetes (N (%))	54 (18.1%)
Hypertension (N (%))	152 (50.8%)
History of Atrial Flutter (N (%))	63 (21.1%)
History of Atrial Tachycardia (N (%))	7 (2.3%)
Prior Myocardial Infarction (N (%))	4 (1.3%)
Prior Stroke/Transient Ischemic Attack (N (%))	30 (10.0%)
History of Coronary Artery Disease (N (%))	28 (9.4%)



Korea Cohort Procedural Characteristics

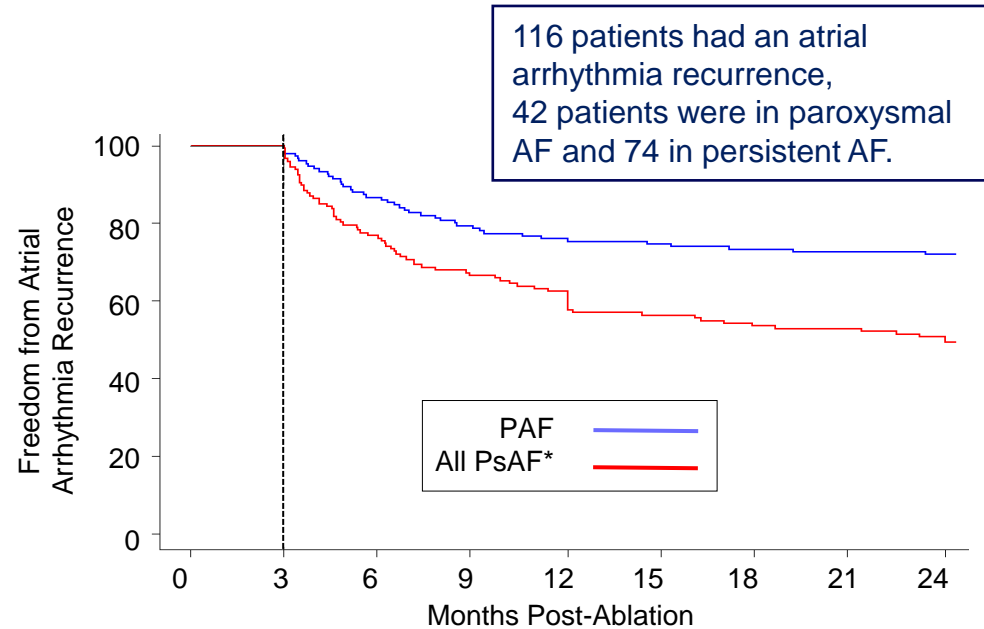
Procedural Characteristics (N=299)	
Total Lab Occupancy Time (Min)	114 ± 24
Total Procedure Time (Min)	76 ± 21
Left Atrial Dwell Time (Min)	56 ± 23
Total Fluoroscopy Time (Min)	27 ± 23
Sedation Method	
-General	195 (65.2%)
-Conscious	104 (34.8%)
Pre-procedural Mapping CT or MRI	191 (63.9%)
Intra-procedural 3D Electroanatomical Mapping	0 (0.0%)
Intracardiac Echocardiography	157 (52.5%)
Cavotricuspid Isthmus (CTI) Ablation	66 (22.1%)
Other Non-PV Ablations	8 (2.7%)
-Left Atrial AF Trigger(s)	4 (1.3%)
- Superior Vena Cava Trigger(s)	2 (0.7%)
-Other (1 PSVT, 1 LV Anterior Wall Ablation)	2 (0.7%)
Acute Pulmonary Vein Isolation Success	293 (98.0%)
Esophageal Monitored at Least One Vein	199 (66.6%)
Phrenic Nerve Monitoring	299 (100.0%)



24-Months Efficacy & Safety

Freedom from AF/AFL/AT at 24 months:

- Paroxysmal AF: 71.9% (95% CI: 64.0 – 78.4%)
- All Persistent AF: 49.3% (95% CI: 41.0 – 57.1%)



Number at Risk	0	3	6	9	12	15	18	21	24
PAF	150	150	130	119	114	110	107	106	105
All PsAF*	149	147	112	98	91	82	78	76	73

Serious Procedure-Related Adverse Events:

- 111 total adverse events reported in 81 subjects
 - 2 events were **serious index procedure-related** in two subjects (0.7%).
- No AE fistula, pericardial tamponade, or PV stenosis were reported
 - One death was reported during the 24-month follow-up, not related to the device or procedure.




Serious Procedure-Related Adverse Events	(N Subjects with Events, % Subjects)
Total	2, 0.7%
Incision Site Hematoma	1, 0.3%
Vascular Pseudoaneurysm	1, 0.3%

AF = atrial fibrillation, AFL = atrial flutter, AT = atrial tachycardia

*PsAF and LsPsAF patient data pooled



24-Months Healthcare Utilization

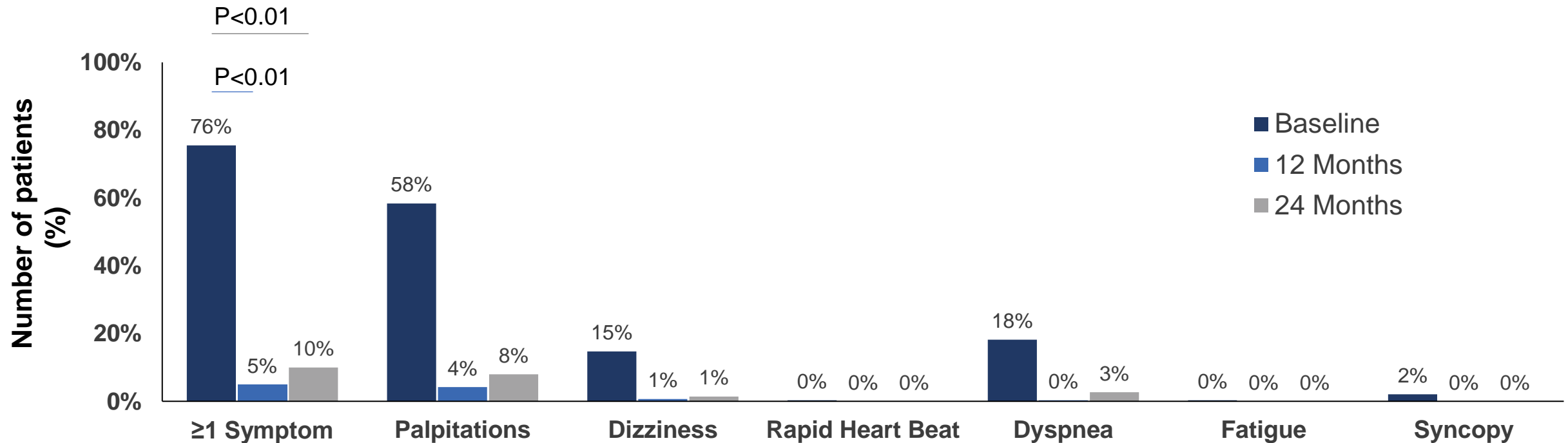
24-Month Healthcare Utilization			
Freedom from	 Repeat Ablations	 Cardiovascular Hospitalization	 Cardioversions
Paroxysmal AF	93.9%	91.3%	98.0%
All Persistent AF	81.4%	72.5%	94.5%

Kaplan-Meier estimates



24-Months AF Symptoms

- Percentage of patients with symptoms significantly reduced post ablation



24-Months Quality of Life (EQ-5D)

- Overall quality of life (measured by EQ-5D questionnaire) significantly improved post ablation

	QOL (N=285 ¹)			
	Baseline	12-months	24-months	p-value ²
EQ-5D index	0.82 ± 0.23	0.90 ± 0.20	0.93 ± 0.16	< 0.01
Visual analogue scale (VAS)	74 ± 17	80 ± 13	81 ± 12	< 0.01

¹ 285 / 299 subjects completed an EQ-5D questionnaire at all visits (baseline, 12-month and 24 month)

² Repeated measures mixed model slope over time



Conclusions

In Korean patients with AF, CBA resulted in:

- a high level of longer-term freedom from health care utilization in both paroxysmal and persistent AF patients
- a clinically significant improvement in AF-related symptoms and quality of life
- Positive safety profile (0.7% serious procedure-related adverse events)



Thank you!

Houng-beom Ahn, MD

On behalf of the Cryo Global Registry investigators



Baseline Characteristics

Baseline Patient Characteristics	PAF (N = 150)	All PsAF* (N = 149)	Total Subjects (N = 299)
Age (years, mean \pm SD)	60 \pm 11	61 \pm 10	60 \pm 11
Female Sex (N(%))	40 (26.7%)	34 (22.8%)	74 (24.7%)
Diagnosed with AF (years, mean \pm SD)	2.3 \pm 2.8	3.3 \pm 3.1	2.8 \pm 3.0
Number of Failed AADs (mean \pm STD)	1.2 \pm 0.7	1.2 \pm 0.5	1.2 \pm 0.6
BMI (kg/m ² , mean \pm SD)	25 \pm 3	25 \pm 3	25 \pm 3
Left Ventricular Ejection Fraction (%; mean \pm SD)	61 \pm 7	57 \pm 9	59 \pm 8
Left Atrial Diameter (mm; mean \pm SD)	41 \pm 6	45 \pm 7	43 \pm 7
CHA ₂ DS ₂ -VASc Score (mean \pm SD)	1.7 \pm 1.4	2.0 \pm 1.4	1.8 \pm 1.4
Diabetes (N(%))	23 (15.3%)	31 (20.8%)	54 (18.1%)
Hypertension (N(%))	64 (42.7%)	88 (59.1%)	152 (50.8%)
History of Atrial Flutter (N(%))	35 (23.3%)	28 (18.8%)	63 (21.1%)
History of Atrial Tachycardia (N(%))	6 (4.0%)	1 (0.7%)	7 (2.3%)
Prior Myocardial Infarction (N(%))	1 (0.7%)	3 (2.0%)	4 (1.3%)
Prior Stroke/Transient Ischemic Attack (N(%))	16 (10.7%)	14 (9.4%)	30 (10.0%)
History of Coronary Artery Disease (N(%))	21 (14.0%)	7 (4.7%)	28 (9.4%)

*PsAF and LsPsAF patient data pooled

Procedural Characteristics

Procedure Characteristics	PAF (N = 150)	All PsAF * (N = 149)	Total Subjects (N = 299)
Total Procedure Time ¹ (minutes, mean ±SD)	71 ± 17	82 ± 23	76 ± 21
Left Atrial Dwell Time ² (minutes, mean ±SD)	48 ± 17	63 ± 25	56 ± 23
Total Fluoroscopy Time (minutes, mean ±SD)	23 ± 14	31 ± 29	27 ± 23
Esophageal Temperature Monitored (N(%))	117 (78.0%)	78 (52.3%)	195 (65.2%)
Phrenic Nerve Monitored (N(%))	150 (100.0%)	149 (100.0%)	299 (100.0%)
Pre-procedural CT or MRI (N(%))	84 (56.0%)	107 (71.8%)	191 (63.9%)
Intracardiac Echocardiography (N(%))	64 (42.7%)	93 (62.4%)	157 (52.5%)
Successful PVI (N(%))	146 (97.3%)	147 (98.7%)	293 (98.0%)
Non-PV Ablations (N(%))	4 (2.7%)	4 (2.7%)	8 (2.7%)
-Left-sided Trigger	1 (0.7%)	3 (2.0%)	4 (1.3%)
-Superior Vena Cava Trigger	2 (1.3%)	0 (0.0%)	2 (0.7%)
-Other (1 PSVT, 1 LV Anterior Wall Ablation)	1 (0.7%)	1 (0.7%)	2 (0.7%)
Cavotricuspid Isthmus (CTI) Ablation (N(%))	28 (18.7%)	38 (25.5%)	66 (22.1%)

¹ Total procedure time is defined as time of first venous access to time of last cryocatheter removal

² Left atrium dwell time is defined as time from first cryoablation catheter insertion to last cryoablation catheter removal

Atrial Arrhythmia Recurrence

- AF was the most common type of first atrial arrhythmia recurrence during 24-months of follow-up.

Distribution of First Recurrent Arrhythmia Type

		PAF (N = 150)	All PsAF * (N = 149)	Total Subjects (N = 299)
Number of Patients with Recurrence		42 (28.0%)	74 (49.7%)	116 (38.8%)
Recurrence Arrhythmia Type	AF	20 (13.3%)	62 (41.6%)	82 (27.4%)
	AFL	6 (4.0%)	6 (4.0%)	12 (4.0%)
	AT	13 (8.7%)	4 (2.7%)	17 (5.7%)
	AF and AFL	1 (0.7%)	1 (0.7%)	2 (0.7%)
	AF and AT	2 (1.3%)	1 (0.7%)	3 (1.0%)

AF = atrial fibrillation, AFL = atrial flutter, AT = atrial tachycardia
 *PsAF and LsPsAF patient data pooled

Procedural Characteristics

Cryo Energy application

Cryo Energy Application	Total (N=299)
Total Veins Treated (N)	1209
Number of Applications per Vein (mean ±SD)	1.5 ± 1.0
Duration of Cryoapplications (sec, mean ±SD)	167 ± 54
Cryoballoon Nadir Temp (°C, mean ±SD)	-49.9 ± 6.8

Discharge

Length of stay	PAF (N = 150)	All PsAF * (N = 149)	Total Subjects (N = 299)
Same Day Discharge (N(%))	0 (0.0%)	0 (0.0%)	0 (0.0%)
1 Day (N(%))	138 (92.0%)	141 (94.6%)	279 (93.3%)
2 Days (N(%))	9 (6.0%)	6 (4.0%)	15 (5.0%)
3+ Days (N(%))	3 (2.0%)	2 (1.3%)	5 (1.7%)

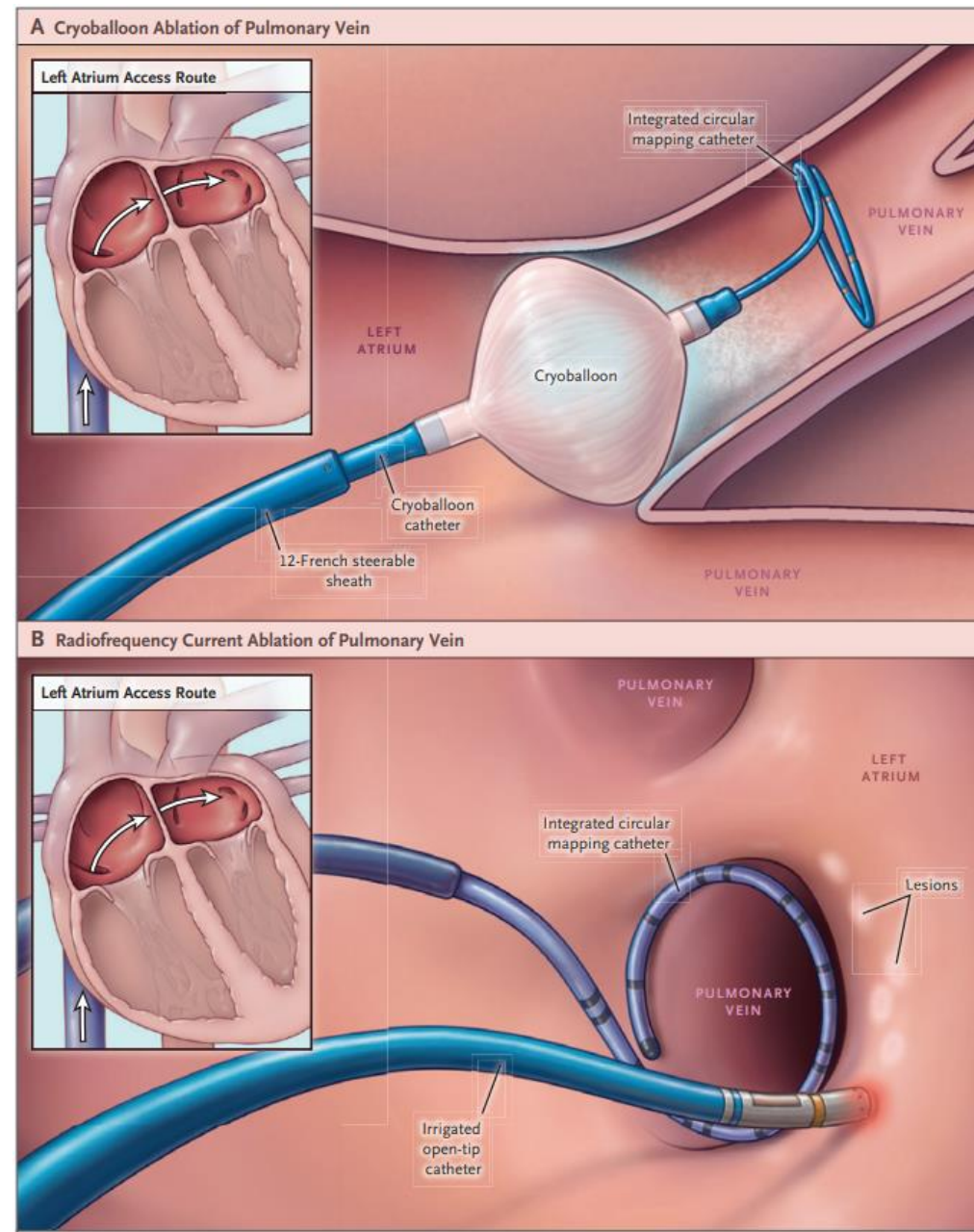
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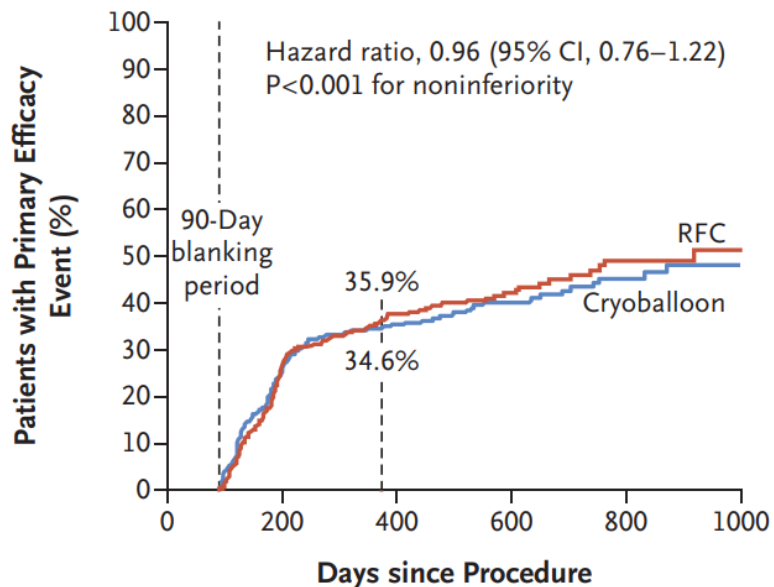
ORIGINAL ARTICLE

Cryoballoon or Radiofrequency Ablation for Paroxysmal Atrial Fibrillation

Karl-Heinz Kuck, M.D., Josep Brugada, M.D., Alexander Fürnkranz, M.D., Andreas Metzner, M.D., Feifan Ouyang, M.D., K.R. Julian Chun, M.D., Arif Elvan, M.D., Ph.D, Thomas Arentz, M.D., Kurt Bestehorn, M.D., Stuart J. Pocock, Ph.D., Jean-Paul Albenque, M.D., Ph.D., and Claudio Tondo, M.D., Ph.D., for the FIRE AND ICE Investigators*



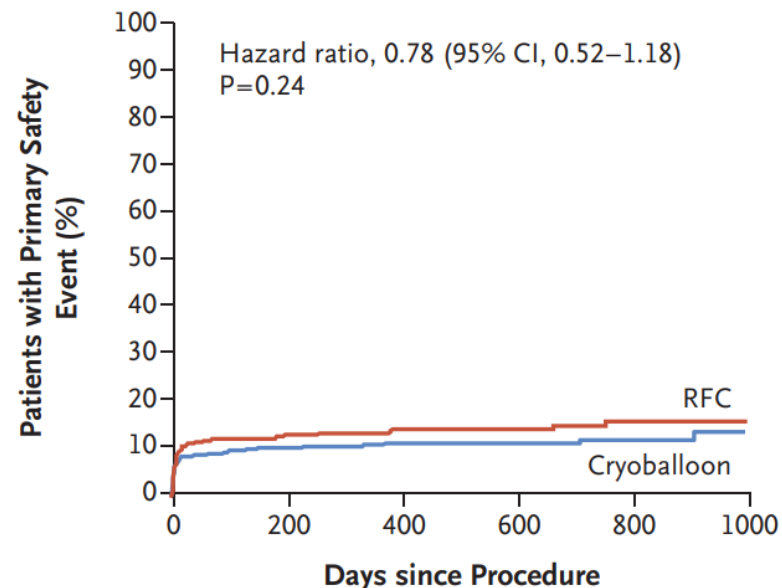
A Primary Efficacy End Point



No. at Risk

Cryoballoon	374	338	242	194	165	132	107	70	57	34	12
RFC	376	350	243	191	149	118	93	58	44	25	12

C Primary Safety End Point



No. at Risk

Cryoballoon	374	323	298	261	229	189	159	117	94	55	21
RFC	376	315	292	247	215	176	146	110	87	52	27

- Primary efficacy end point occurred in 138 patients in the cryoballoon group and in 143 patients in the radiofrequency group (1-year Kaplan–Meier event-rate estimates, 34.6% and 35.9%, respectively; hazard ratio, 0.96; 95% confidence interval [CI], 0.76 to 1.22; $P < 0.001$ for noninferiority)
- Primary safety end point occurred in 40 patients in the cryoballoon group and in 51 patients in the radiofrequency group (1-year Kaplan–Meier event rate estimates, 10.2% and 12.8%, respectively; hazard ratio, 0.78; 95% CI, 0.52 to 1.18; $P = 0.24$)



Cryoballoon or radiofrequency ablation for symptomatic paroxysmal atrial fibrillation: reintervention, rehospitalization, and quality-of-life outcomes in the FIRE AND ICE trial

Karl-Heinz Kuck^{1*}, Alexander Fürnkranz², K.R. Julian Chun², Andreas Metzner¹, Feifan Ouyang¹, Michael Schlüter¹, Arif Elvan³, Hae W. Lim⁴, Fred J. Kueffer⁴, Thomas Arentz⁵, Jean-Paul Albenque⁶, Claudio Tondo⁷, Michael Kühne⁸, Christian Sticherling⁸, and Josep Brugada⁹, on behalf of the FIRE AND ICE Investigators

¹Department of Cardiology, Asklepios Klinik St. Georg, Lohmühlenstr. 5, 20099 Hamburg, Germany; ²Cardioangiologisches Centrum Bethanien, Frankfurt, Germany; ³Isala Klinieken, Zwolle, The Netherlands; ⁴Medtronic, Inc., Minneapolis, MN, USA; ⁵Herz-Zentrum, Bad Krozingen, Germany; ⁶Clinique Pasteur, Toulouse, France; ⁷Centro Cardiologico Monzino, University of Milan, Milan, Italy; ⁸Universitätsspital Basel, Basel, Switzerland; and ⁹Hospital Clinic, University of Barcelona, Barcelona, Spain

Table 1 Summary of rehospitalization data

	Total number of events; subjects with events		Hazard ratio (95% CI)	P-value
	Cryoballoon (n = 374)	RFC (n = 376)		
All-cause rehospitalizations	210; 122 (32.6%)	267; 156 (41.5%)	0.72 (0.57–0.91)	0.01
Cardiovascular rehospitalizations	139; 89 (23.8%)	203; 135 (35.9%)	0.61 (0.47–0.80)	<0.01
Repeat ablations	49; 44 (11.8%)	70; 66 (17.6%)	0.65 (0.45–0.95)	0.03
Direct-current cardioversions	13; 12 (3.2%)	28; 24 (6.4%)	0.49 (0.25–0.98)	0.04

Table 2 Summary of Short Form-12 and EuroQol five-dimension three-level data out to 6 and 12 months

Survey	Group ^a	Baseline	6 months				12 months		
			n	6 months	Difference	P-value ^b	n	12 months	Difference
SF-12 mental	Cryoballoon	47.1 ± 10.3	258	51.1 ± 8.9	4.0 ± 9.8	<0.01	236	51.2 ± 9.4	3.7 ± 10.6
	RFC	48.9 ± 9.8	267	50.8 ± 8.8	1.9 ± 9.9	<0.01	230	50.7 ± 9.2	1.6 ± 10.8
SF-12 physical	Cryoballoon	43.7 ± 9.1	258	47.0 ± 9.1	3.2 ± 8.2	<0.01	236	47.0 ± 9.2	3.0 ± 8.7
	RFC	44.5 ± 9.5	267	47.6 ± 8.6	3.1 ± 8.6	<0.01	230	47.8 ± 8.4	3.3 ± 8.7
EQ-5D-3L	Cryoballoon	0.85 ± 0.14	274	0.89 ± 0.13	0.03 ± 0.14	<0.01	257	0.88 ± 0.13	0.03 ± 0.14
	RFC	0.87 ± 0.12	287	0.88 ± 0.14	0.02 ± 0.14	0.03	254	0.88 ± 0.13	0.01 ± 0.14

^aA linear mixed model was utilized to compare groups across all study visits. No differences were observed between arms in quality-of-life metrics.

^bt-Test, change from baseline to 6 months.

- When comparing cryoballoon and RFC catheter ablation in symptomatic patients with paroxysmal AF, this study demonstrated statistically significant and clinically relevant advantages for patients treated with cryoballoon ablation in terms of repeat ablations, DCCVs, all-cause rehospitalizations, and cardiovascular rehospitalizations. Both patient groups improved in quality-of-life scores after AF ablation