



Comparison of Early (≤ 6 months) versus Late (> 6 months) Cryoballoon Ablation From Diagnosis of Atrial Fibrillation: Results From Korean Cryoballoon Ablation Registry

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Introduction

- AF is the most common sustained cardiac arrhythmia in adults

LIFETIME RISK for AF
1 in 3 individuals



of European ancestry
at index age of 55 years
37.0% (34.3% to 39.6%)

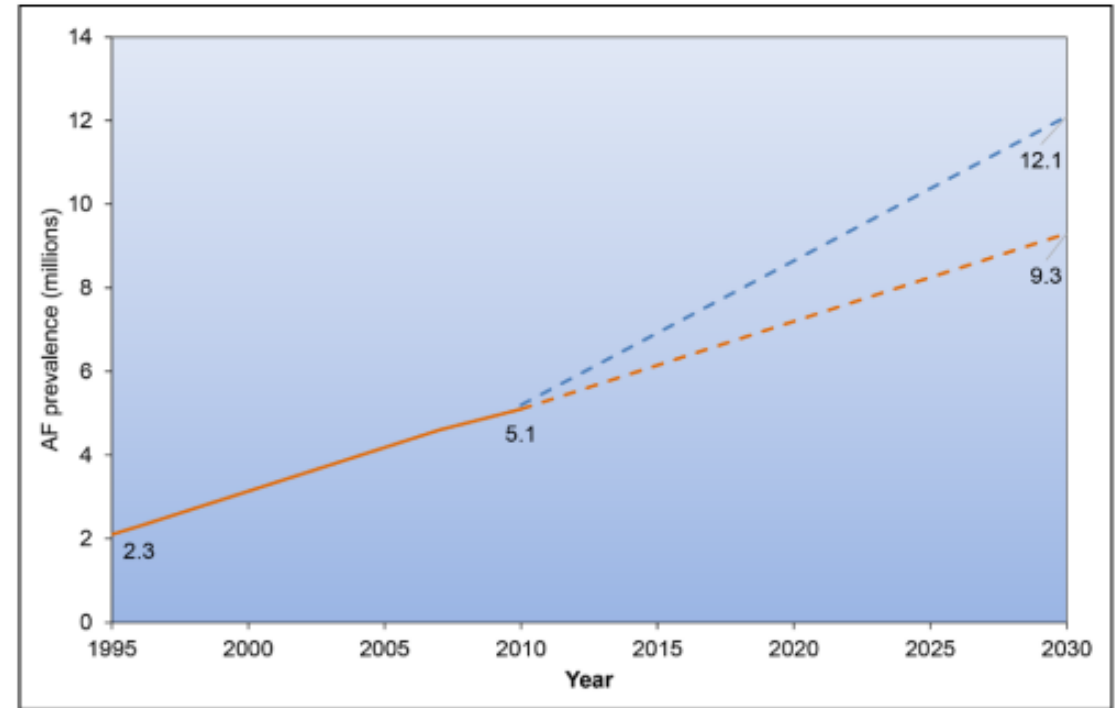


Chart 16-4. Current and future US prevalence projections for AF.

Projections assume no increase (red dashed line) or logarithmic growth (blue dashed line) in incidence of AF from 2007.

AF indicates atrial fibrillation.

Data derived from Go et al¹⁸; and modified from Colilla et al¹⁹ with permission from Elsevier. Copyright © 2013, Elsevier Inc.

Introduction

- AF is progressive and degenerative disease

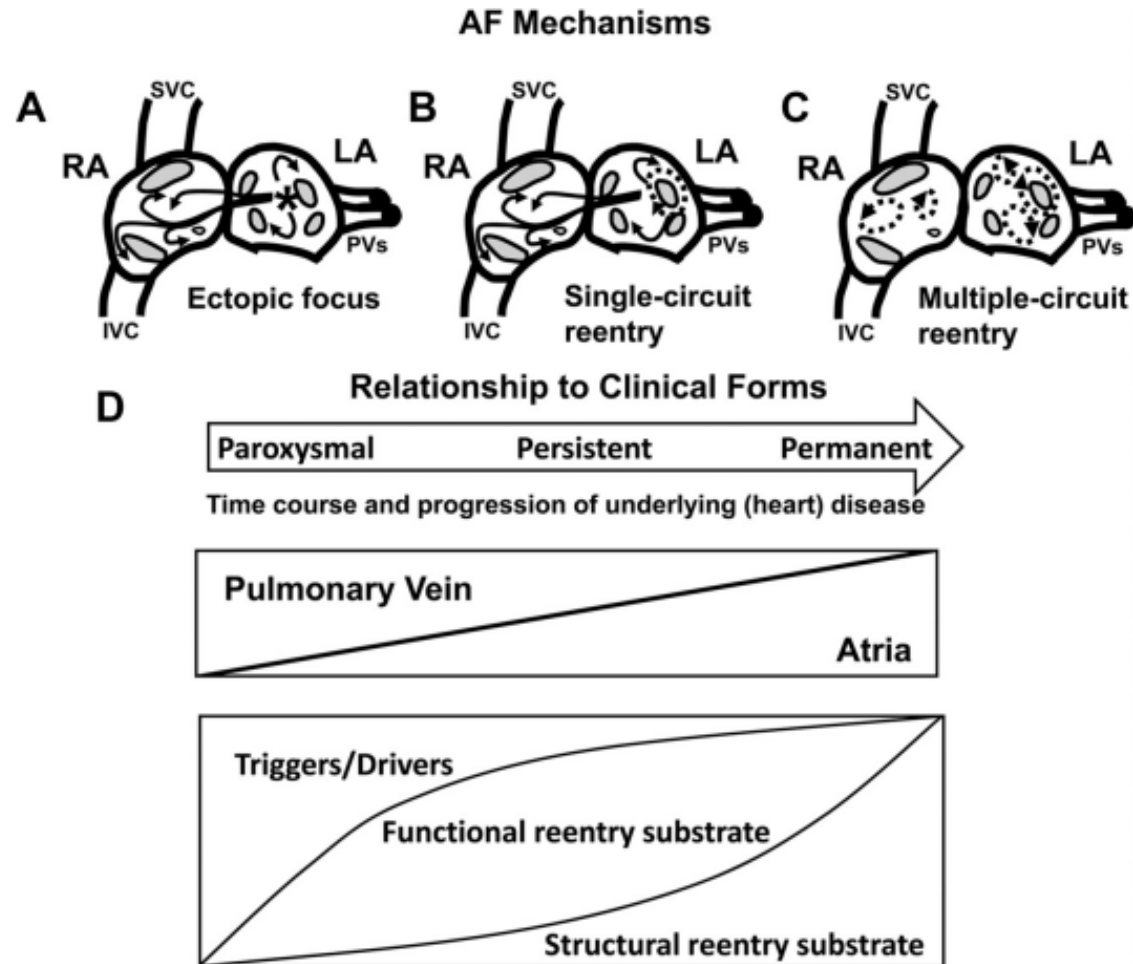
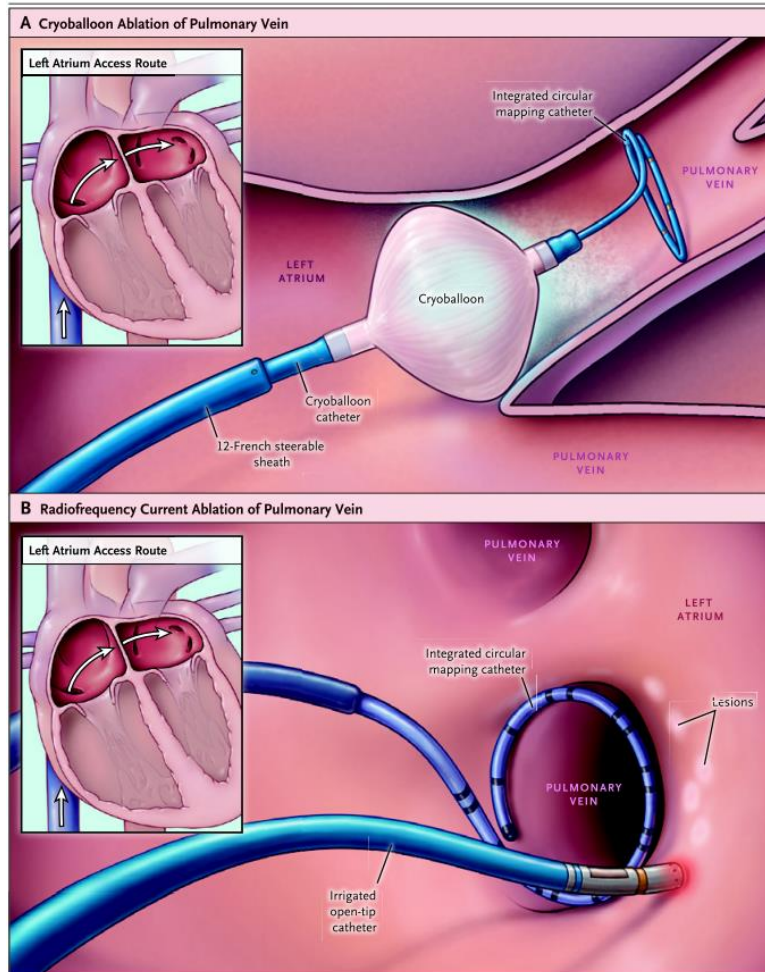


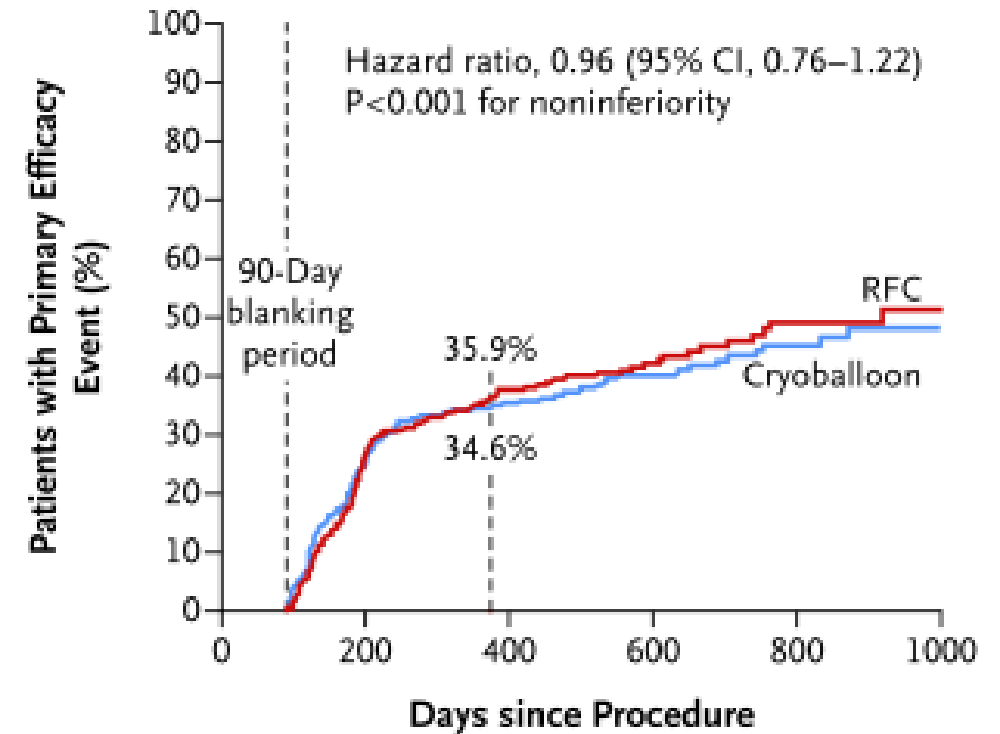
Figure 1. Principal atrial fibrillation (AF)–maintaining mechanisms. **A**, Local ectopic firing. **B**, Single-circuit reentry. **C**, Multiple-circuit reentry. **D**, Clinical AF forms and relation to mechanisms. Paroxysmal forms show a predominance of local triggers/drivers, particularly from pulmonary veins (PVs). As AF becomes more persistent and eventually permanent, reentry substrates (initially functional and then structural) predominate. RA indicates right atrium; SVC, superior vena cava; LA, left atrium; and IVC, inferior vena cava.

Introduction

- Cryoballoon ablation (CBA) is an emerging alternative technique for pulmonary vein isolation.



A Primary Efficacy End Point

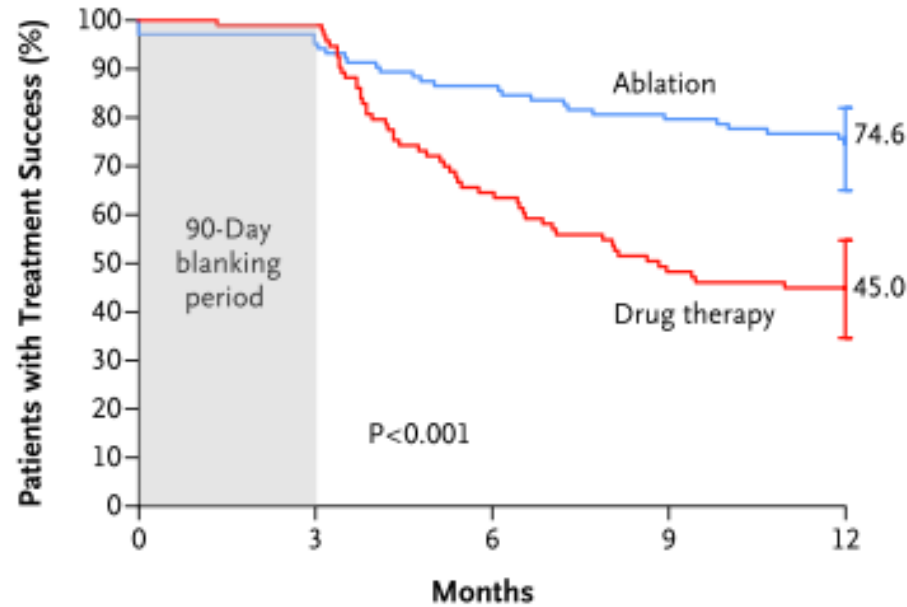


No. at Risk
Cryoballoon
RFC

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

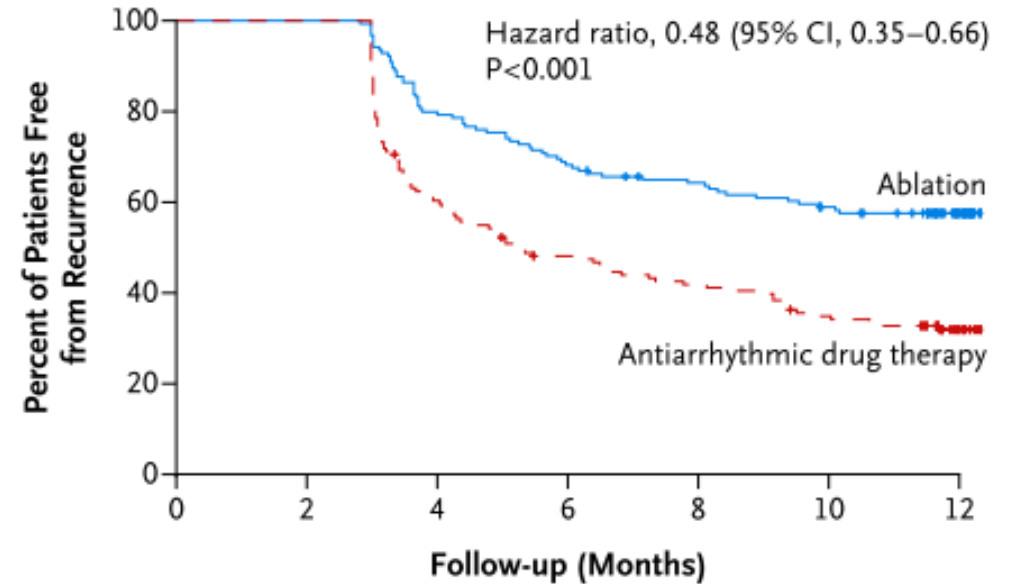
Introduction

- CBA is superior to drug therapy for the prevention of atrial arrhythmia recurrence in patients with PAF



No. at Risk	0	3	6	9	12
Ablation	104	99	88	81	70
Drug therapy	99	93	60	44	39

N Engl J Med. 2021 Jan 28;384(4):316-324.



No. at Risk	0	2	4	6	8	10	12
Ablation	154	154	123	105	96	86	55
Antiarrhythmic drug therapy	149	149	89	69	60	49	27

N Engl J Med. 2021 Jan 28;384(4):305-315.

Introduction

- **Question**
- What is the optimal timing of catheter ablation (CA)?

Introduction

- Shorter duration between time of first AF diagnosis and AF ablation is associated with an increased likelihood of ablation procedural success.

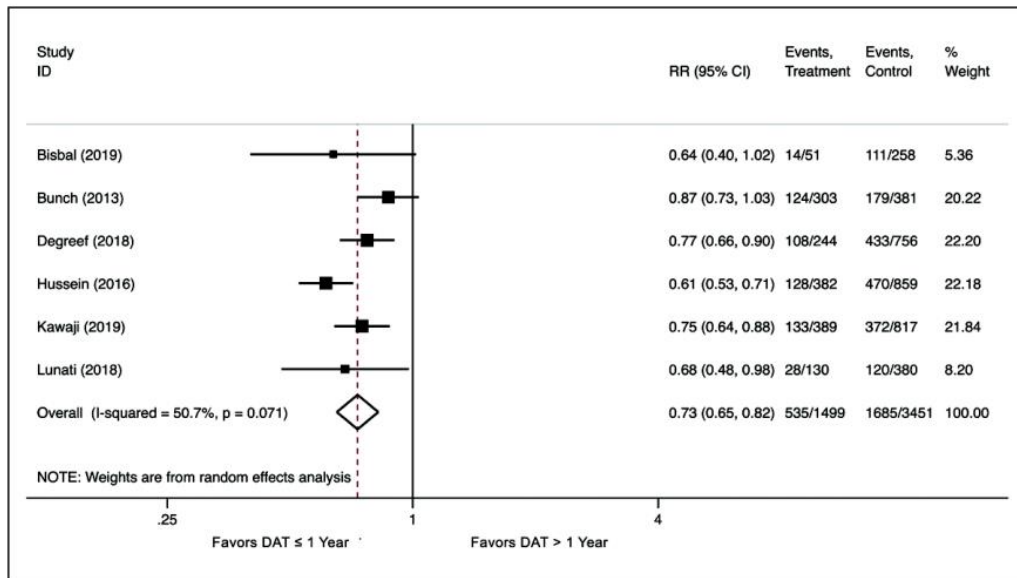


Figure 2. Forest plot showing recurrence of atrial fibrillation after catheter ablation stratified by diagnosis-to-ablation time ≤1 y vs >1 y.

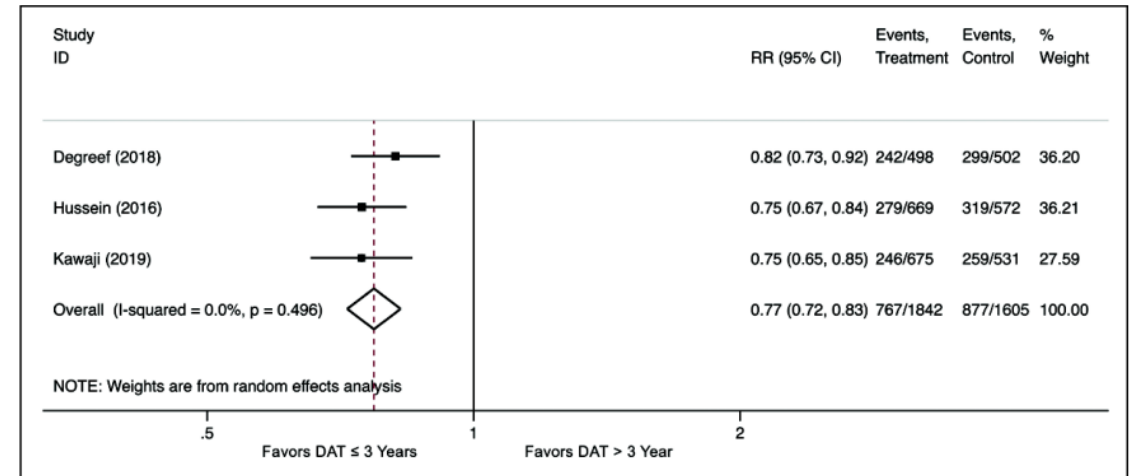


Figure 3. Forest plot showing recurrence of atrial fibrillation after catheter ablation stratified by diagnosis-to-ablation time ≤3 y vs >3 y. DAT indicates diagnosis-to-ablation time.

In this meta-analysis of observational studies, a **diagnosis-to-ablation time of 1 year or less** is associated with a **27% lower risk in atrial fibrillation recurrence post-ablation.**

Introduction

- In strategy with CBA for PV isolation, is early CBA associated with an likelihood of better procedural outcome?

Objective

- We sought to evaluate long-term outcome according to early (≤ 6 months) vs. late (> 6 months) CBA from diagnosis of AF.

Methods

- Using the data from a multicenter registry of cryoballoon ablation for AF in Korea between May 01, 2018, and June 30, 2022
- 2,659 patients were included.
- 84 patients were excluded.
 - < 3 months of FU duration after CBA (N = 48)
 - Have data errors (N = 36)
- Finally, 2,605 patients were included in analysis.

Methods

- **Definition**

- Early (≤ 6 months) CBA = duration from diagnosis of AF to CBA was less than 6 months.
- Late (> 6 months) CBA = duration from diagnosis of AF to CBA was more than 6 months.

- **Primary outcome** = late recurrence of atrial tachyarrhythmia including atrial fibrillation, atrial flutter, or atrial tachycardia longer than 30 seconds, after 3 months of blanking period.

Methods

- **Statistical analysis**
- All statistical analyses and model development were performed using SPSS software (version 26; SPSS Inc., Chicago, IL, USA)
- All tests were two-tailed, and statistical significance was defined as p values ≤ 0.05 .
- A multivariable Cox proportional hazard model was performed to evaluate predictors of AT recurrence during follow-up.
- Kaplan–Meier analysis and log-rank tests were used to assess time-dependent variables.

Results

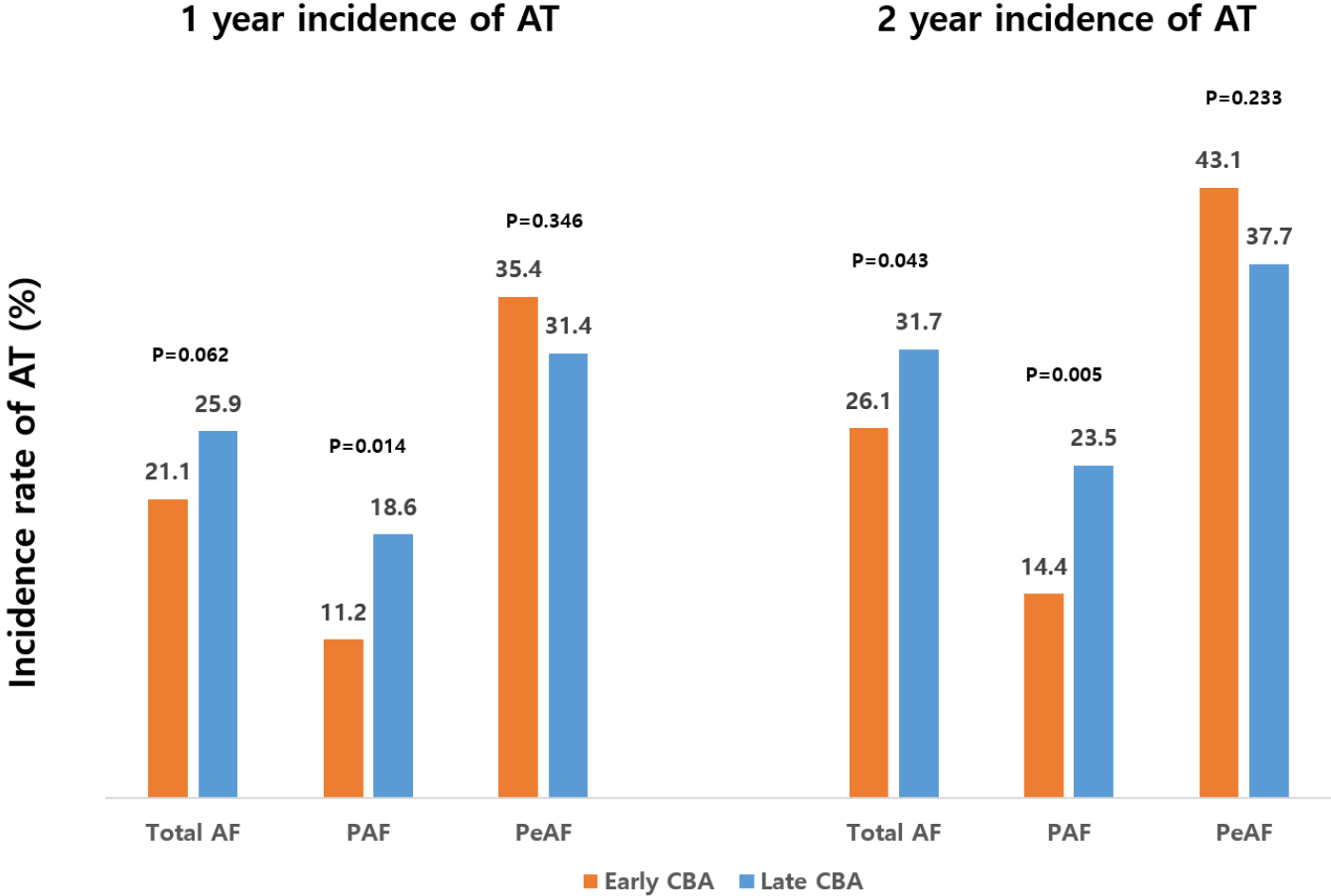
- The baseline characteristics of the study cohort
- 1 year and 2 year AT incidence after CBA
- Predictors of 2 year AT recurrence
- Kaplan-Meier survival curves for AT recurrence within 1 year
- Kaplan-Meier survival curves for AT recurrence within 2 years

The baseline characteristics of the study cohort

	Total (N=2605)	Early CBA (N=318)	Late CBA (N=2287)	P- value
Age, years	61.7 ± 10.0	60.9 ± 10.0	61.8 ± 10.0	0.138
Female, n (%)	607 (23.3)	87 (27.4)	520 (22.7)	0.068
Body mass index, kg/m ²	25.7 ± 3.4	25.6 ± 3.3	25.7 ± 3.4	0.828
Creatinine, mg/dl	1.00 ± 0.62	0.90 ± 0.22	1.01 ± 0.66	<0.001
eGFR, ml/min/1.73m ²	81.8 ± 18.3	85.5 ± 15.8	81.3 ± 18.5	<0.001
Persistent AF, n (%)	1444 (55.4)	130 (40.9)	1314 (57.5)	<0.001
AF duration, days	1140 ± 1211	117 ± 42	1281 ± 1227	<0.001
Hypertension, n (%)	1500 (57.6)	169 (53.1)	1331 (58.2)	0.088
Diabetes, n (%)	560 (21.5)	53 (16.7)	507 (22.2)	0.025
Chronic kidney disease, n (%)	204 (7.8)	15 (4.7)	189 (8.3)	0.027
Heart failure, n (%)	618 (23.7)	53 (16.7)	565 (24.7)	0.002
Coronary artery disease, n (%)	210 (8.1)	26 (8.2)	184 (8.0)	0.936
Myocardial infarction, n (%)	34 (1.3)	6 (1.9)	28 (1.2)	0.295
Stroke/TIA, n (%)	308 (11.8)	28 (8.8)	280 (12.2)	0.075
HCMP, n (%)	58 (2.2)	9 (2.8)	49 (2.1)	0.436
†MS or MV surgery, n (%)	26 (1.0)	2 (0.6)	24 (1.0)	0.762
CHA₂DS₂VASc score	2.1 ± 1.5	1.9 ± 1.4	2.1 ± 1.5	0.002
LA diameter, mm	43.7 ± 6.9	42.3 ± 6.5	44.0 ± 6.9	<0.001
LAVI, ml/m²	49.8 ± 18.7	47.1 ± 17.2	50.1 ± 18.9	0.010
LVEF, %	58.6 ± 8.7	59.8 ± 8.3	58.5 ± 8.8	0.011
CTI ablation, n (%)	574 (22.0)	71 (22.3)	503 (22.0)	0.893

Comparison of 1 year & 2 year AT incidences

- Mean FU duration = 639 ± 306 days



Predictors of 2 year AT recurrence in all AF patients

	Univariate		Multivariate	
	HR (95% CI)	P-value	HR (95% CI)	P-value
Age	0.997 (0.990-1.004)	0.382		
Female	1.018 (0.865-1.197)	0.831		
BMI, kg/m ²	1.018 (0.865-1.197)	0.831		
Persistent AF	1.956 (1.687-2.269)	<0.001	1.631 (1.362-1.953)	<0.001
Early CBA	0.845 (0.673-1.060)	0.145		
Hypertension	0.883 (0.769-1.015)	0.080	0.737 (0.630-0.860)	<0.001
Diabetes	0.966 (0.815-1.145)	0.690		
Heart failure	0.958 (0.847-1.170)	0.958		
Chronic kidney disease	0.963 (0.743-1.247)	0.774		
Coronary artery disease	0.832 (0.634-1.091)	0.184		
Myocardial infarction	0.796 (0.413-1.535)	0.496		
Stroke/TIA	1.046 (0.848-1.289)	0.675		
HCMP	1.598 (1.096-2.330)	0.015		
†MS or MV surgery	1.804 (1.043-3.121)	0.035		
CHA ₂ DS ₂ VASc score	0.964 (0.921-1.009)	0.115		
LA diameter, mm	1.055 (1.044-1.065)	<0.001	1.030 (1.016-1.045)	<0.001
LAVI, ml/m²	1.017 (1.014-1.020)	<0.001	1.008 (1.004-1.013)	<0.001
LV EF, %	0.992 (0.985-1.000)	0.043		
CTI ablation	0.684 (0.569-0.822)	<0.001	0.718 (0.579-0.892)	0.003

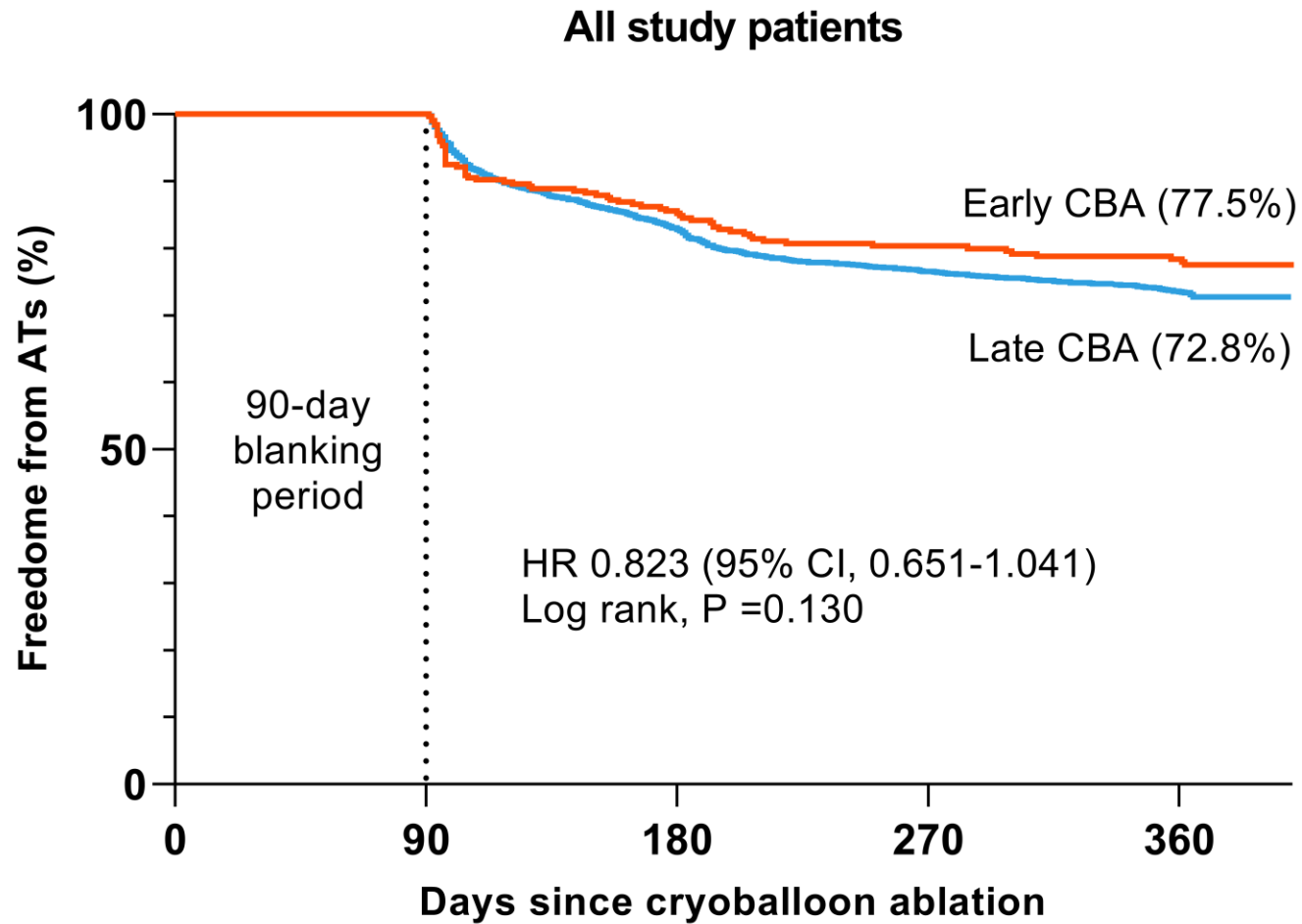
Predictors of 2 year AT recurrence in PAF patients

	Univariate		Multivariate	
	HR (95% CI)	P-value	HR (95% CI)	P-value
Age	0.995 (0.984-1.007)	0.401		
Female	0.910 (0.688-1.202)	0.506		
BMI, kg/m ²	1.026 (0.989-1.064)	0.172		
Early CBA	0.628 (0.421-0.935)	0.022	0.637 (0.412-0.984)	0.042
Hypertension	0.856 (0.670-1.094)	0.215		
Diabetes	0.749 (0.524-1.070)	0.112		
Heart failure	1.614 (1.190-2.189)	0.002		
Chronic kidney disease	1.036 (0.663-1.619)	0.877		
Coronary artery disease	0.887 (0.556-1.416)	0.615		
Myocardial infarction	0.417 (0.104-1.677)	0.218		
Stroke/TIA	1.158 (0.811-1.655)	0.419		
HCMP	3.313 (1.810-6.064)	<0.001	2.472 (1.238-4.939)	0.010
†MS or MV surgery	3.653 (1.170-11.407)	0.026		
CHA ₂ DS ₂ VASc score	0.974 (0.899-1.055)	0.523		
LA diameter, mm	1.067 (1.044-1.090)	<0.001		
LAVI, ml/m²	1.013 (1.005-1.022)	0.003	1.010 (1.001-1.019)	0.027
LV EF, %	0.978 (0.964-0.991)	0.001	0.980 (0.966-0.995)	0.009
CTI ablation	1.200 (0.916-1.572)	0.186		

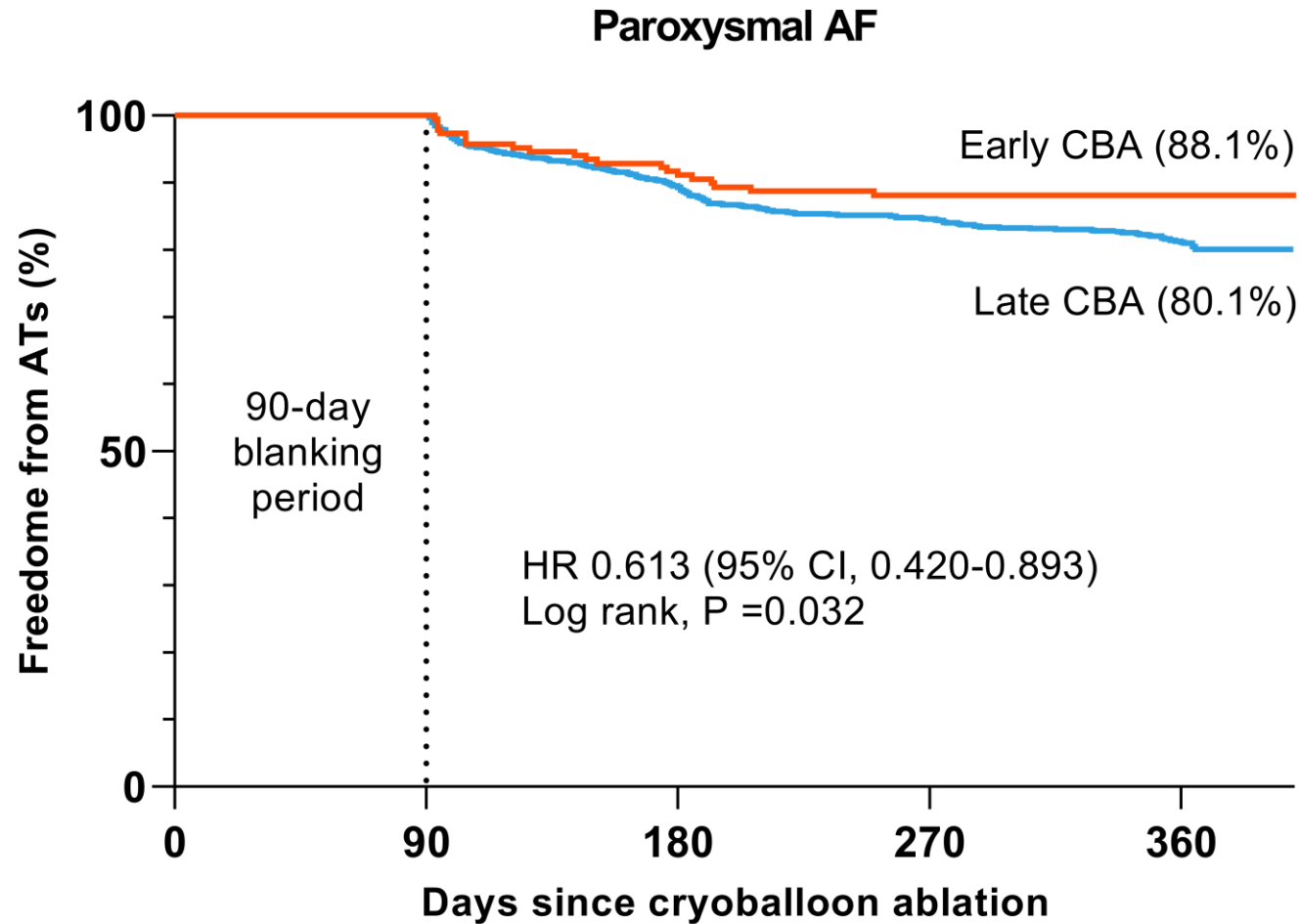
Predictors of 2 year AT recurrence in PeAF patients

	Univariate		Multivariate	
	HR (95% CI)	P-value	HR (95% CI)	P-value
Age	0.996 (0.987-1.005)	0.364		
Female	1.232 (1.008-1.504)	0.041		
BMI, kg/m ²	0.988 (0.964-1.013)	0.342		
Early CBA	1.233 (0.936-1.626)	0.137		
Hypertension	0.793 (0.669-0.939)	0.007	0.773 (0.408-0.748)	0.006
Diabetes	0.952 (0.784-1.157)	0.622		
Heart failure	0.688 (0.568-0.833)	<0.001	0.604 (0.488-0.748)	<0.001
Chronic kidney disease	0.926 (0.674-1.273)	0.636		
Coronary artery disease	0.810 (0.580-1.131)	0.217		
Myocardial infarction	1.295 (0.614-2.729)	0.497		
Stroke/TIA	1.001 (0.772-1.296)	0.996		
HCMP	1.042 (0.643-1.689)	0.867		
†MS or MV surgery	1.280 (0.685-2.392)	0.440		
CHA ₂ DS ₂ VASc score	0.931 (0.880-0.985)	0.013		
LA diameter, mm	1.034 (1.021-1.047)	<0.001		
LAVI, ml/m²	1.013 (1.010-1.017)	<0.001	1.013 (1.008-1.018)	<0.001
LV EF, %	1.008 (0.999-1.018)	0.086		
CTI ablation	0.491 (0.377-0.638)	<0.001	0.553 (0.408-0.749)	<0.001

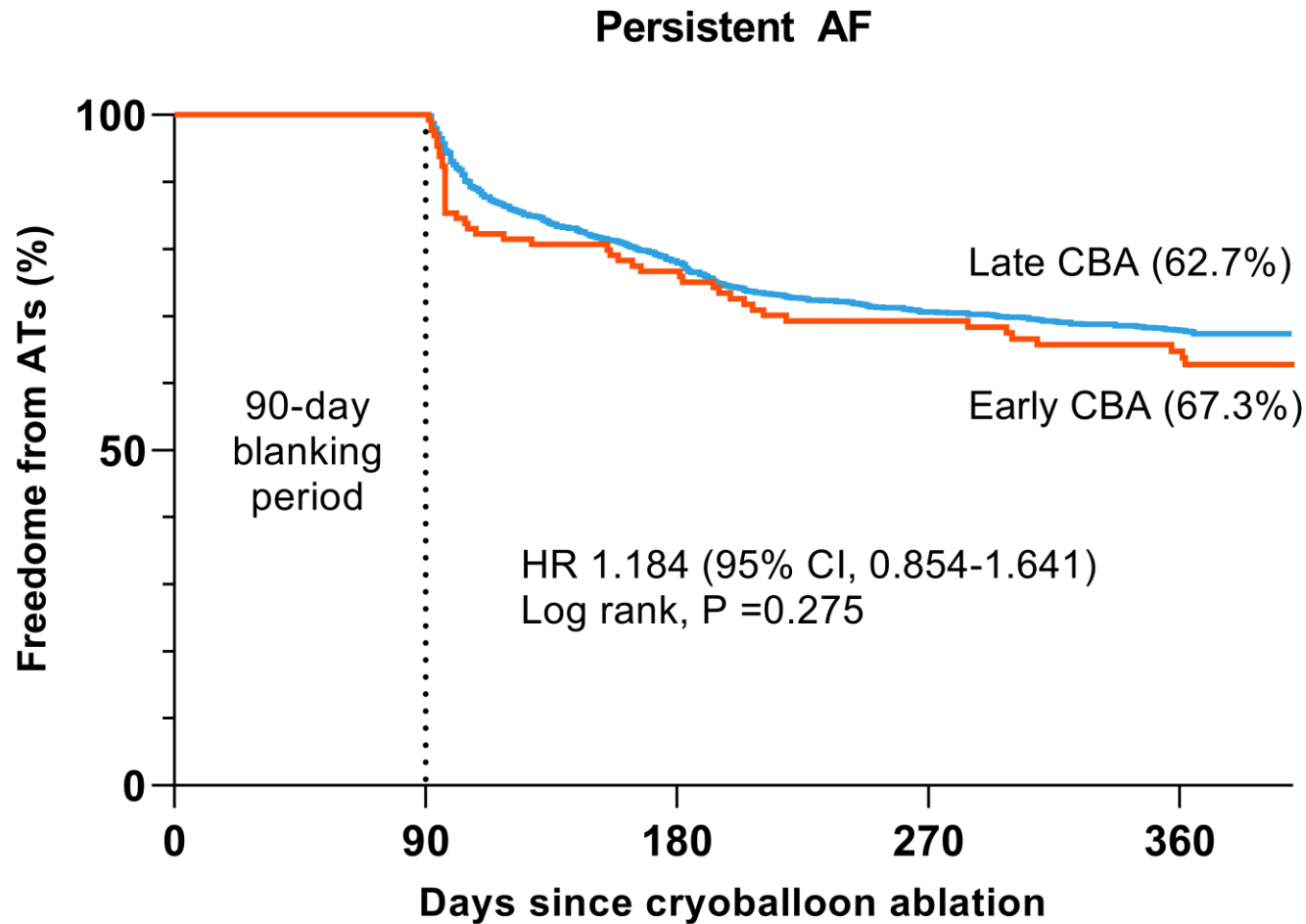
Kaplan-Meier survival curves for AT recurrence within 1 year



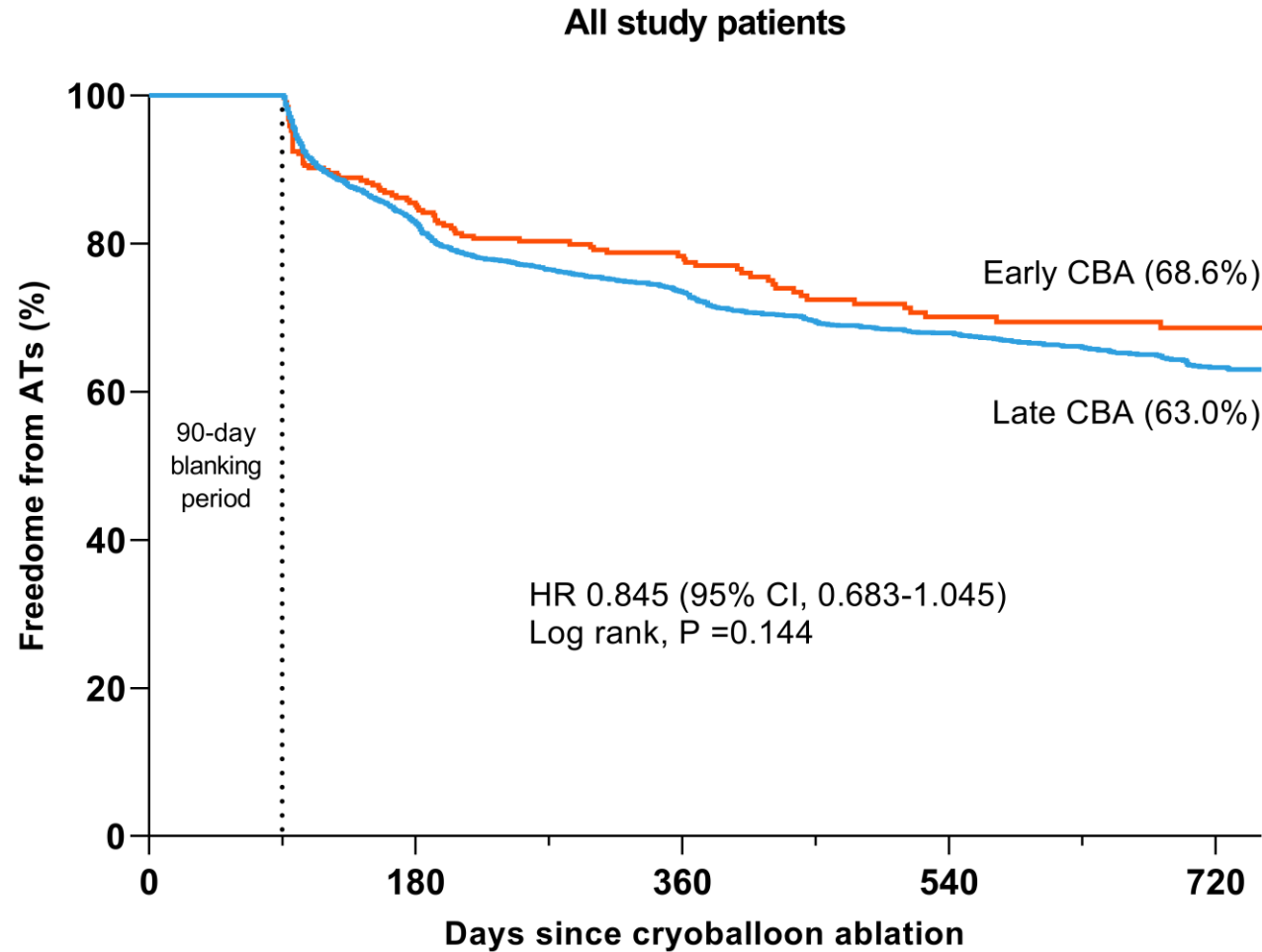
Kaplan-Meier survival curves for AT recurrence within 1 year



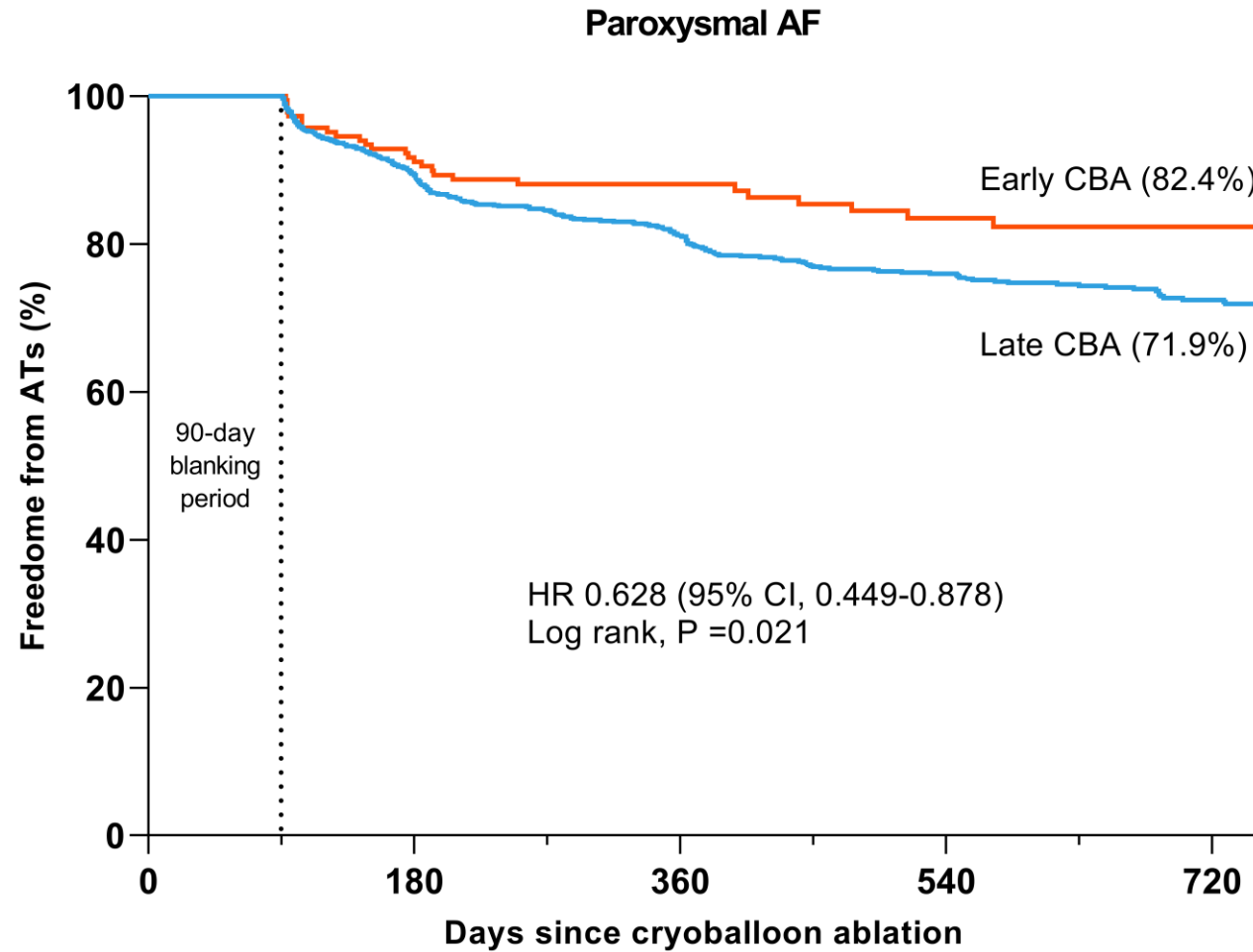
Kaplan-Meier survival curves for AT recurrence within 1 year



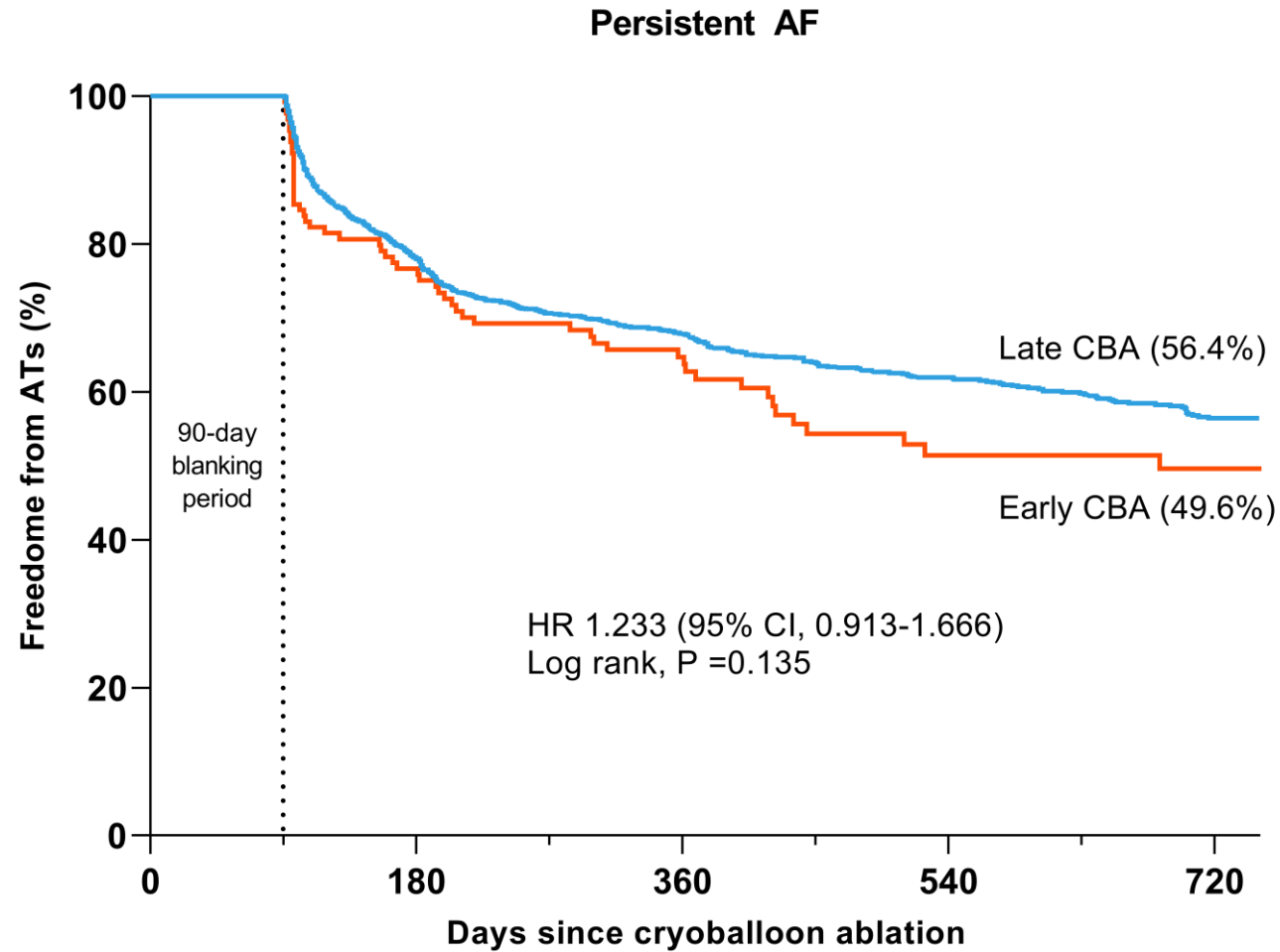
Kaplan-Meier survival curves for AT recurrence within 2 years



Kaplan-Meier survival curves for AT recurrence within 2 years



Kaplan-Meier survival curves for AT recurrence within 2 years



Major findings of study

- Early (≤ 6 months) CBA from diagnosis of AF did not show a significant reduction of 1 year and 2 years AT recurrences after blanking period compared to late (> 6 months) CBA in total AF patients.
- However, early CBA significantly reduced 1 year & 2 year AT recurrences compared to late CBA in PAF patients, but not in PeAF patients.

Clinical implication

- PeAF itself is a significant predictor of AT recurrence after CBA.
- Early CBA is effective to prevent recurrence of AT in PAF patients, but not in PeAF patients.
- We need to do CA for PAF patients as soon as possible, and to prevent the progression from PAF to PeAF.
 - Early detection of AF recurrence with smart watch, wearable patch, or ILR.

Limitations

- Retrospective studies
- AF diagnosis date \neq AF initiation date
- Unadjusted AAD effect
- Heterogeneity of FU monitoring for AT recurrence after CBA

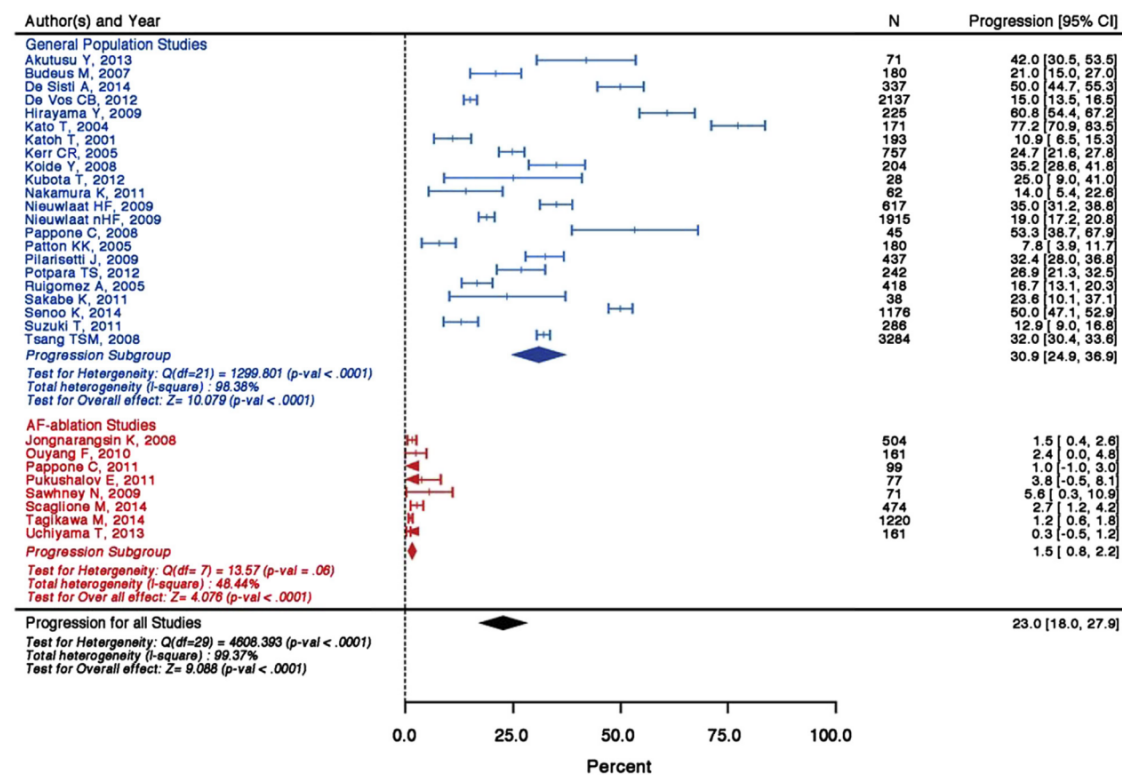
Discussion

A Systematic Review on the Progression of Paroxysmal to Persistent Atrial Fibrillation

Shedding New Light on the Effects of Catheter Ablation

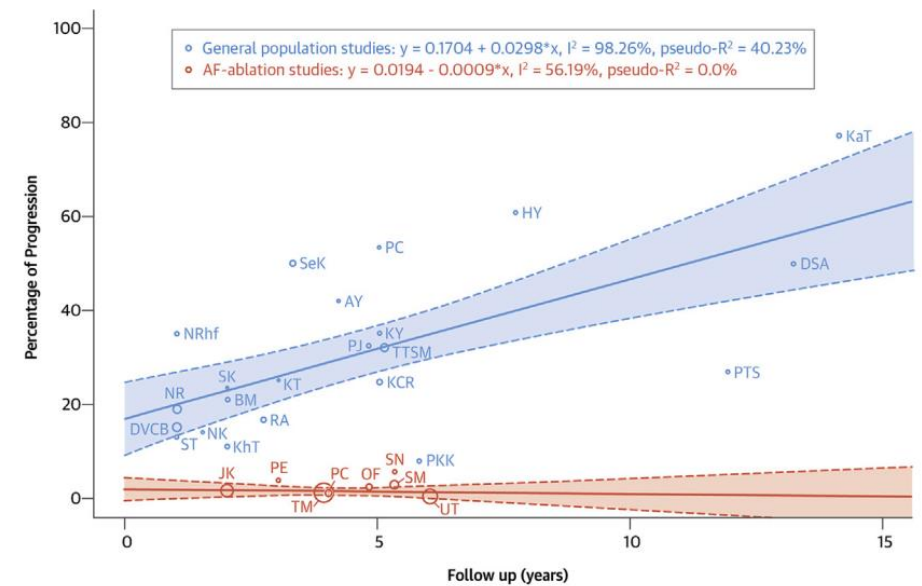
Riccardo Proietti, MD, PhD,*† Alexios Hadjis, BSc, MD,* Ahmed AlTurki, MD,* George Thanassoulis, MD, MSc,* Jean-François Roux, MD,‡ Atul Verma, MD,§ Jeff S. Healey, MD,|| Martin L. Bernier, MD,* David Birnie, MD,¶ Stanley Nattel, MD,# Vidal Essebag, MD, PhD***

FIGURE 2 Forest Plot for Percentage of Progression of AF in All Studies Divided Into 2 Groups (General Population and AF Ablation)



CI = confidence interval; other abbreviation as in Figure 1.

CENTRAL ILLUSTRATION Weighted Progression of AF as a Function of Duration of Follow-Up in General Population and AF Ablation Studies



Proietti, R. et al. J Am Coll Cardiol EP. 2015; 1(3):105-15.

The labels are the initials of the names of the studies included in Figure 2. AF = atrial fibrillation.

Progression of Atrial Fibrillation after Cryoablation or Drug Therapy

- 303 patients with PAF
- CBA (n = 154) vs. AAD (n = 149)
- 3-year follow-up
- FU with ILR

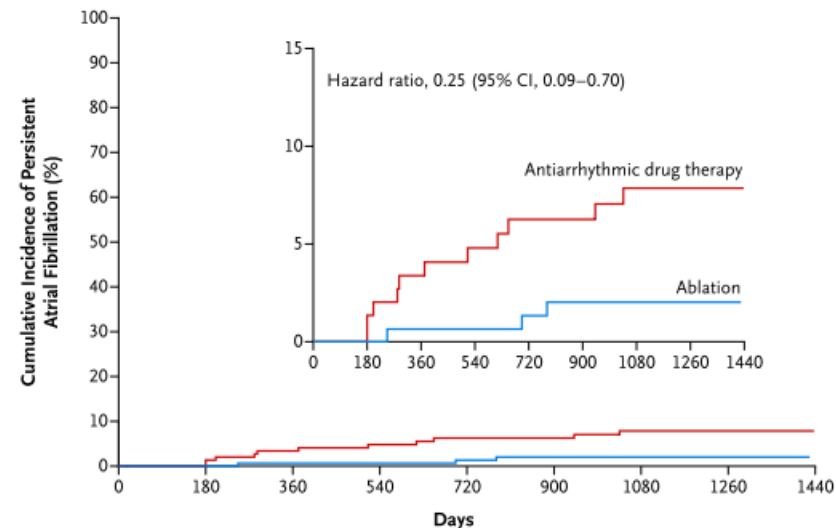
Table 1. Main End Points of Interest.*

End Point	Ablation Group (N=154)	Antiarrhythmic Drug Group (N=149)	Hazard Ratio (95% CI)
	<i>number (percent)</i>		
Progression to persistent atrial fibrillation from 91 days after treatment initiation to final follow-up	3 (1.9)	11 (7.4)	0.25 (0.09–0.70)
Recurrence of any atrial tachyarrhythmia			
From 91 days to 12 mo after treatment initiation†	66 (42.9)	101 (67.8)	0.48 (0.35–0.66)
From 91 days to 36 mo after treatment initiation	87 (56.5)	115 (77.2)	0.51 (0.38–0.67)

* Observed data are shown in the trial-group columns. The hazard ratio is a model-based effect estimate and was calculated with a Cox regression analysis. Because the statistical analysis plan did not include a provision for correcting for multiplicity when conducting tests for secondary or other outcomes, results are reported as point estimates and 95% confidence intervals. The widths of the confidence intervals have not been adjusted for multiplicity, so the intervals should not be used to infer definitive treatment effects for secondary outcomes.

† Data were previously reported by Andrade et al.¹¹

J.G. Andrade, M.W. Deyell, L. Macle, G.A. Wells, M. Bennett, V. Essebag, J. Champagne, J.-F. Roux, D. Yung, A. Skanes, Y. Khaykin, C. Morillo, U. Jolly, P. Novak, E. Lockwood, G. Amit, P. Angaran, J. Sapp, S. Wardell, S. Lauck, J. Cadrin-Tourigny, S. Kochhäuser, and A. Verma, for the EARLY-AF Investigators*



No. at Risk	180	360	540	720	900	1080	1260	1440	
Antiarrhythmic drug therapy	149	148	142	133	129	123	104	43	0
Ablation	154	154	153	151	145	141	125	43	0

Figure 2. Cumulative Incidence of First Episode of Persistent Atrial Fibrillation.

Shown is a time-to-event analysis of the first occurrence of persistent atrial fibrillation, as documented by the implantable cardiac monitor between 91 days after the initiation of treatment (receipt of antiarrhythmic drug or catheter ablation) and final trial follow-up. The inset shows the same data on an enlarged y axis.

Impact of early vs. delayed atrial fibrillation catheter ablation on atrial arrhythmia recurrences

Jonathan M. Kalman^{1,2,*†}, Ahmed M. Al-Kaisey^{1,2,3†}, Ramanathan Parameswaran^{1,2,3}, Joshua Hawson^{1,2}, Robert D. Anderson^{1,2}, Michael Lim^{1,2}, David Chieng^{3,4}, Stephen A. Joseph¹, Alex McLellan¹, Joseph B. Morton¹, Paul B. Sparks¹, Geoffrey Lee^{1,2}, Prashanthan Sanders⁵, and Peter M. Kistler^{2,3,4}

Table 1 Baseline demographic, clinical and echocardiographic characteristics

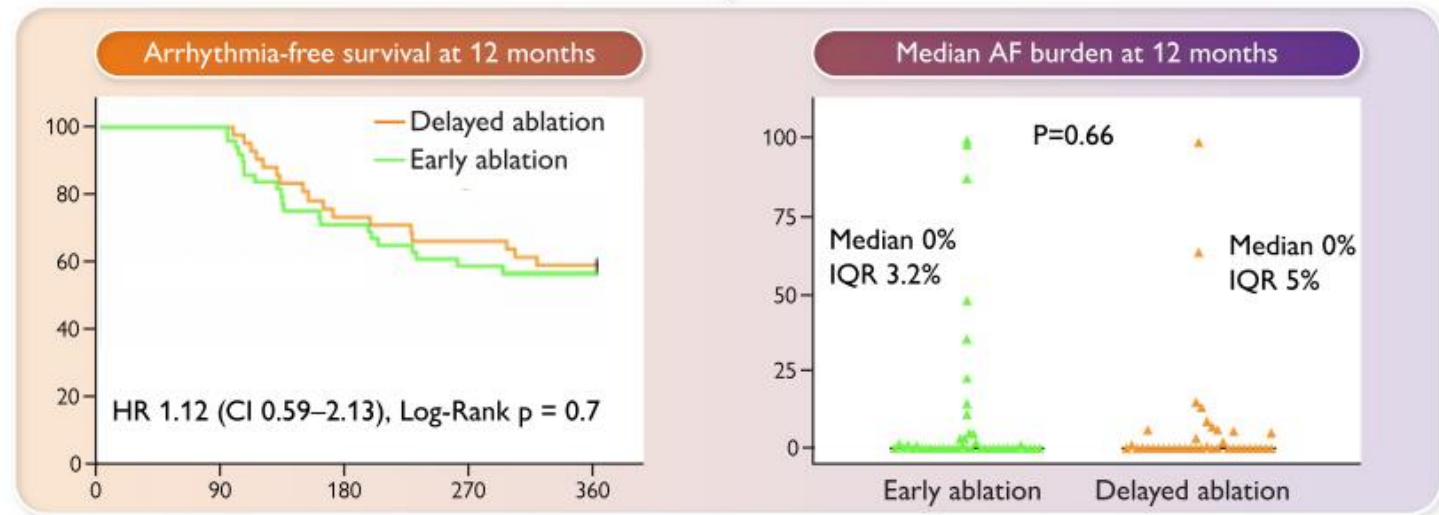
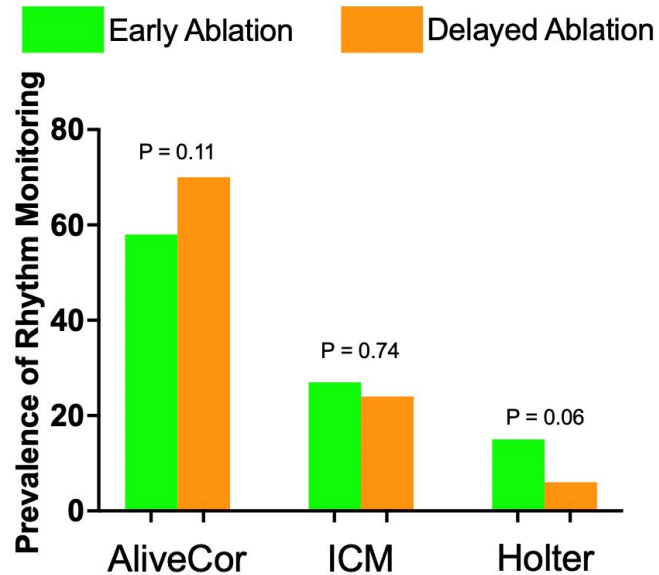
	Early Ablation Group (n = 48)	Delayed Ablation Group (n = 41)
Age, years, mean ± SD	58 ± 13	59 ± 11
Female sex, n (%)	16 (33)	10 (24)
Persistent AF, n (%)	26 (54)	15 (37)

Design

- 100 symptomatic AF patients
- Randomized to either early or delayed ablation strategy
- Intensive postoperative rhythm monitoring for 12 months

Endpoints

- Primary**
- Arrhythmia-free survival at 12 months
- Secondary**
- Median AF burden
 - Median AF burden by AF phenotype
 - AAD use



Conclusion

- In total AF patients, early CBA (≤ 6 months) after diagnosis of AF did not show significant reduction of 2 year AT incidence compared to late CBA.
- However, according to AF progression, early CBA showed significant risk reduction of 2 year AT recurrences in PAF patients, but not in PeAF patients.
- So, early CBA may be needed to prevent AT recurrence and/or disease progression in PAF patients.

Thank you for your kind attention!

