



Rhythm outcome of persistent atrial fibrillation ablation depending on the timing of the first electrocardiographic documentation



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COI Disclosure

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



Background

- Delays in treatment with catheter ablation impact procedural success rates independent of temporal changes to the AF subtype at ablation.

Bunch TJ, et al. Heart Rhythm. 2013 Sep;10(9):1257-62.

- Shorter diagnosis-to-ablation times are associated with better clinical success. Our data advocate for early PVI following diagnosis of AF.

De Greef Y, et al. Europace. 2018 Apr 1;20(4):589-595.

- Although longer AF duration was associated with higher clinical recurrence rates after AFCA, the rate was significant in patients with PeAF lasting >3 years, but not in PAF patients.

Yu HT, et al. J Cardiovasc Electrophysiol. 2020 Feb;31(2):457-464.

- Compared with an early ablation strategy, delaying AF ablation by 12 months for AAD management did not result in reduced ablation efficacy.

Kalman JM, et al. Eur Heart J. 2023 Apr 16:ehad247.



Background

- Delays in treatment with catheter ablation impact procedural success rates independent of temporal changes to the AF subtype at ablation.

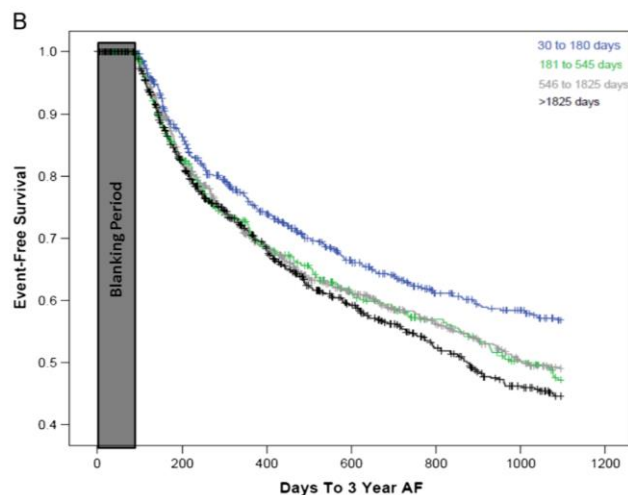
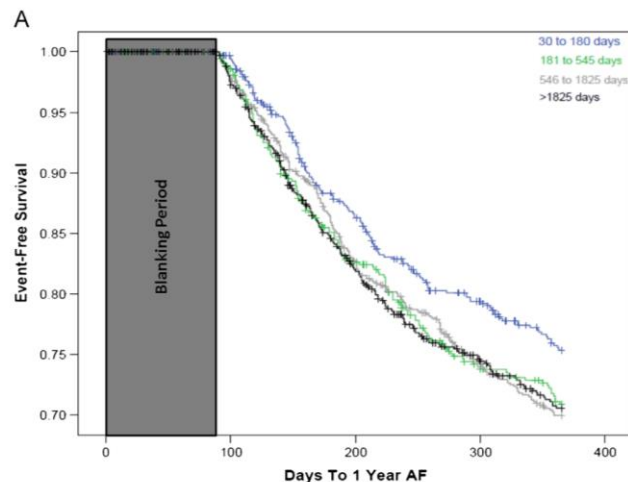


Table 1 Baseline patient demographics separated by the time interval from first known diagnosis of AF and first AF ablation procedure

Characteristic	30–180 days (n = 187)	181–545 days (n = 116)	546–1825 days (n = 186)	> 1825 days (n = 195)	P value
Age (years)	63.7 ± 11.1	62.6 ± 11.8	66.4 ± 10.2	67.6 ± 9.7	< .0001
Sex (male)	62.6%	62.1%	56.5%	64.1%	.45
Hypertension	64.7%	82.8%	74.7%	80.0%	.001
Hyperlipidemia	28.9%	25.9%	36.0%	32.3%	.25
Diabetes	21.4%	25.0%	21.5%	24.6%	.79
Heart failure	19.8%	24.1%	41.4%	31.3%	< .0001
Prior myocardial infarction	4.3%	6.9%	7.5%	8.7%	.37
Prior cerebrovascular accident	2.7%	7.8%	5.9%	7.2%	.18
Prior cardioversion	44.9%	38.8%	35.5%	48.2%	.06
Paroxysmal	56.1%	58.6%	57.0%	59.5%	.92
Persistent	28.3%	25.0%	30.6%	27.2%	.74
Permanent	16.0%	17.2%	12.4%	13.3%	.58
Ejection fraction (%)	51.8 ± 13.1	51.0 ± 13.8	52.3 ± 13.8	54.8 ± 14.0	.001
Coronary artery disease (> 50%)	5.3%	12.9%	17.7%	15.4%	.002
CHADS2					.10
0	23.5%	12.9%	16.1%	14.4%	
1	39.0%	37.1%	34.4%	31.3%	
2	23.5%	28.4%	22.6%	25.6%	
3	11.2%	15.5%	18.3%	16.4%	
4	2.1%	4.3%	6.5%	8.7%	
5	0.5%	1.7%	2.1%	3.6%	
Statin	38.5%	44.8%	44.6%	46.7%	.41
Angiotensin-converting enzyme inhibitor/ angiotensin receptor blocker	41.7%	50.9%	44.6%	47.2%	.44
Acetylsalicylic acid	82.4%	82.8%	80.1%	82.1%	.93
Plavix	4.3%	6.0%	6.5%	4.6%	.76
Diuretic	50.8%	53.4%	53.8%	53.3%	.94
Beta-blocker	39.6%	48.3%	53.2%	50.8%	.05
Calcium channel blocker	23.0%	25.0%	23.7%	24.1%	.98
Digoxin	9.1%	9.5%	11.8%	10.3%	.84
Coumadin	78.1%	76.7%	72.0%	76.9%	.54
Amiodarone	12.8%	13.8%	10.8%	12.3%	.87
Dofetilide	5.9%	2.6%	3.8%	4.6%	.55
Flecainide	18.2%	17.2%	18.8%	18.5%	.99
Propafenone	5.9%	3.4%	4.3%	5.1%	.78
Sotalol	4.8%	6.9%	7.5%	6.7%	.74

AF = atrial fibrillation.



Background

- Shorter diagnosis-to-ablation times are associated with better clinical success. Our data advocate for early PVI following diagnosis of AF.

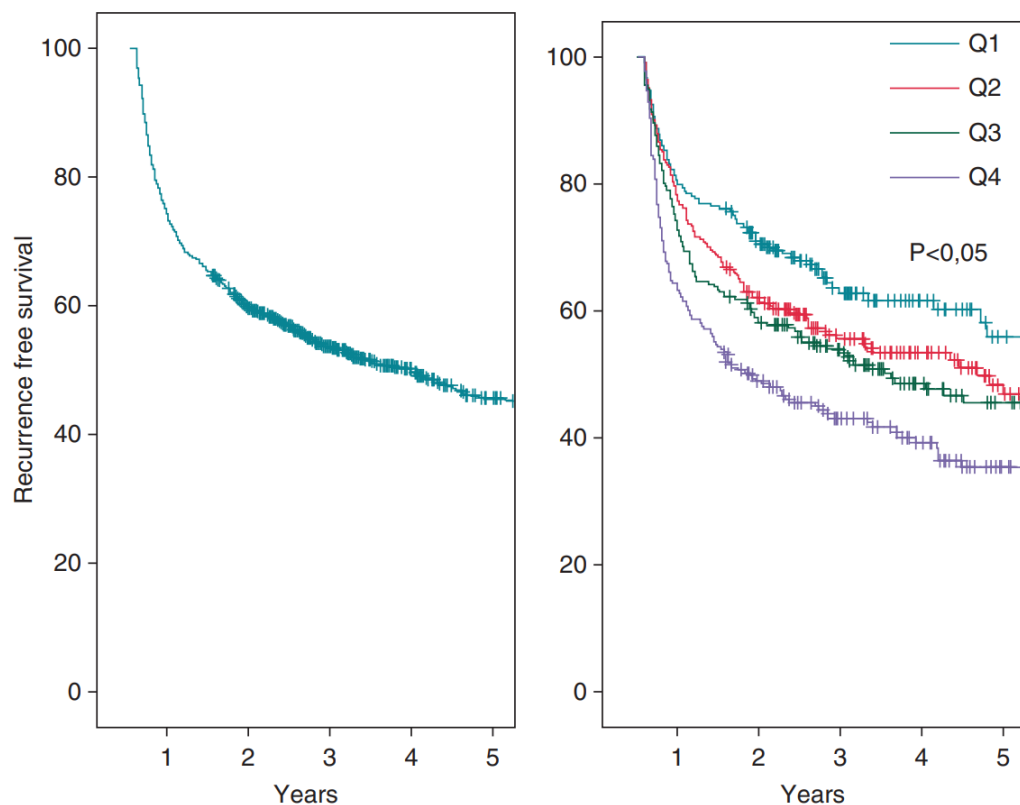


Table 1 Baseline patient characteristics for all patients and DAT subgroups

	All (N=1000)	Q1 (N=244)	Q2 (N=254)	Q3 (N=252)	Q4 (N=250)	P-value
Age (years, ± SD)	60 ± 10	59 ± 10	59 ± 10	60 ± 10	62 ± 10	0.0003
Male (N, %)	717 (72%)	171 (70%)	181 (71%)	179 (71%)	186 (74%)	0.731
Type of AF						
Par AF (N, %)	585 (58.5%)	159 (65.2%)	154 (60.6%)	141 (55.9%)	131 (52.4%)	0.024
Per AF (N, %)	410 (41.0%)	83 (34.0%)	100 (39.4%)	111 (44.0%)	116 (46.4%)	0.027
Lper AF (N, %)	7 (0.7%)	2 (0.8%)	1 (0.4%)	2 (0.8%)	2 (0.8%)	0.927
AHT (N, %)	423 (42.3%)	97 (39.8%)	100 (39.4%)	116 (46%)	110 (44%)	0.351
DM (N, %)	89 (8.9%)	20 (8.2%)	19 (7.5%)	23 (9.1%)	27 (10.8%)	0.591
Prior CV (N, %)	401 (40.1%)	85 (34.8%)	97 (38.2%)	105 (41.7%)	114 (45.6%)	0.086
No. of prior AAD (N, ± SD)	2.1 ± 0.8	1.8 ± 0.7	2.0 ± 0.7	2.2 ± 0.8	2.4 ± 1.0	<0.0001
Prior amiodarone (N, %)	318 (31.8%)	61 (25.0%)	68 (26.6%)	81 (32.1%)	108 (43.2%)	<0.0001
Prior TIA/CVA (N, %)	68 (6.8%)	12 (4.9%)	8 (3.1%)	21 (8.3%)	27 (10.8%)	0.009
LA size (mm, ± SD)	42 ± 7	42 ± 7	42 ± 6	43 ± 7	43 ± 8	0.479
SHD (N, %)	198 (19.8%)	51 (20.9%)	53 (20.9%)	50 (19.8%)	44 (17.6%)	0.770
BMI (kg/m ²)	28 ± 11	28 ± 13	28 ± 15	28 ± 4	28 ± 4	0.868
CHA ₂ DS ₂ -VASc	1 ± 1	1 ± 1	1 ± 1	1 ± 1	2 ± 1	0.022
0	316 (31.7%)	80 (32.9%)	88 (34.8%)	78 (31.0%)	70 (28.0%)	0.015
1	297 (29.8%)	77 (31.7%)	75 (29.6%)	72 (28.6%)	73 (29.2%)	
2	209 (20.9%)	51 (21.0%)	61 (24.1%)	53 (21.0%)	44 (17.6%)	
≥3	176 (17.6%)	35 (14.4%)	29 (11.5%)	49 (19.4%)	63 (25.2%)	
Diagnosis-to-ablation time (months, ±SD)	47 ± 48	6 ± 3	20 ± 6	47 ± 11	116 ± 45	NA
Ablation technique (N, %)						
1. Carto manual	266 (26.6%)	50 (20.5%)	72 (28.3%)	70 (27.8%)	74 (29.6%)	<0.0001
2. Ensite manual	137 (13.7%)	41 (16.8%)	39 (15.4%)	22 (8.7%)	35 (14.0%)	
3. Carto stereotaxis	173 (17.3%)	66 (27.0%)	40 (15.7%)	31 (12.3%)	36 (14.4%)	
4. HDMA mesh	59 (5.9%)	8 (3.3%)	9 (3.5%)	21 (8.3%)	21 (8.4%)	
5. Cryoballoon	93 (9.3%)	29 (11.9%)	23 (9.1%)	22 (8.7%)	19 (7.6%)	
6. PVAC	272 (27.2%)	50 (20.5%)	71 (28.0%)	86 (34.1%)	65 (26.0%)	

Data are presented as the mean value ± SD or number (%) of patients. Q, first AF diagnosis to ablation time quartiles. NS, not significant; NA, non applicable; AAD, antiarrhythmic drug; AHT, arterial hypertension; BMI, body mass index; CV, cardioversion; CVA, cerebrovascular accident; DM, diabetes mellitus; LA, left atrium; LperAF, longstanding persistent AF; ParAF, paroxysmal atrial fibrillation; PerAF, persistent atrial fibrillation; PS-LAX, parasternal long axis view; SHD, structural heart disease; TIA, transient ischemic attack; TTE, transthoracic echocardiogram.



Background

- Although longer AF duration was associated with higher clinical recurrence rates after AFCA, the rate was significant in patients with PeAF lasting >3 years, but not in PAF patients.

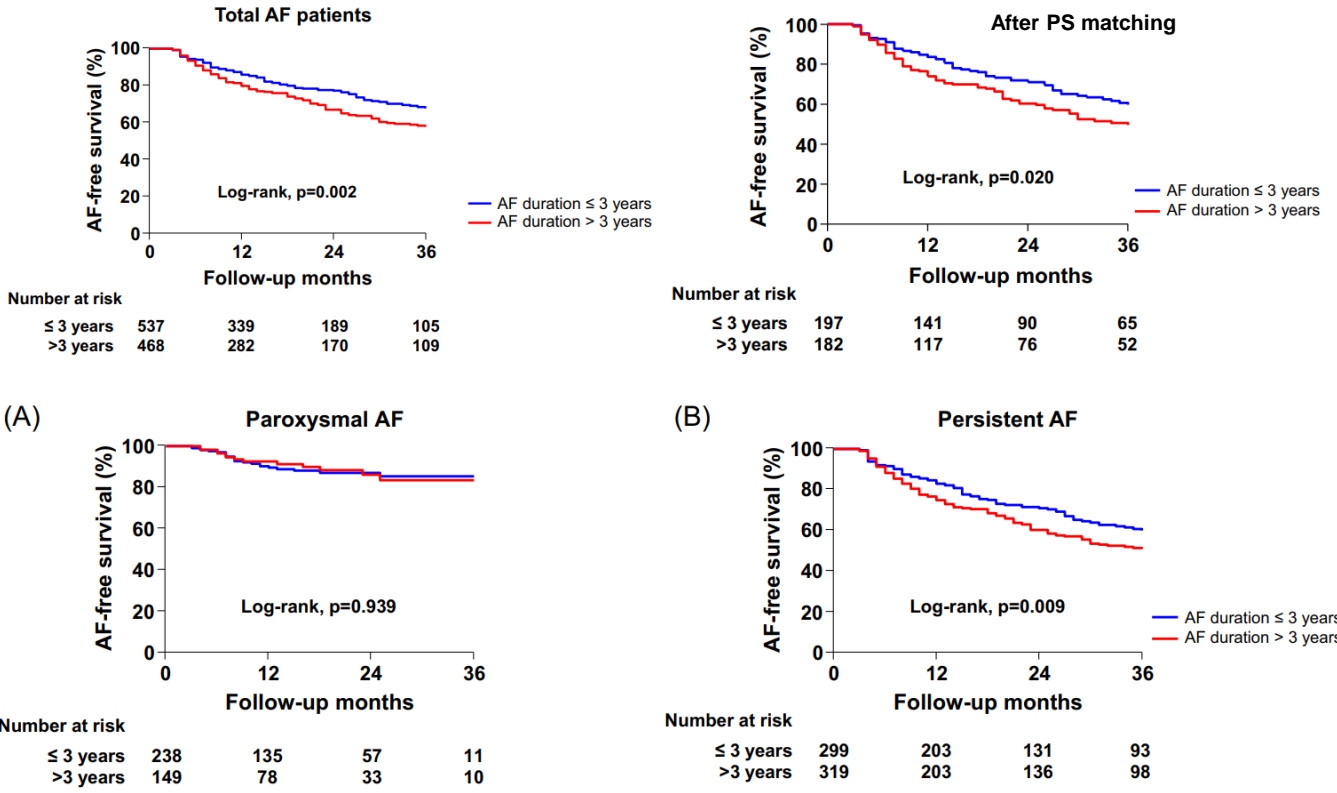


TABLE 1 Baseline characteristics of the patients

	AF duration ≤ 3 y (n = 537)	AF duration > 3 y (n = 468)	P value
Age, y	58.2 ± 11.2	59.7 ± 10.0	.020*
Male sex, n (%)	391 (72.8)	363 (77.6)	.083
Paroxysmal AF, n (%)	238 (44.3)	149 (31.8)	<.001*
BSA, m ²	1.81 ± 0.19	1.82 ± 0.18	.795
BMI, kg/m ²	25.1 ± 3.1	25.0 ± 3.4	.529
Comorbidities			
Heart failure, n (%)	75 (14.0)	66 (14.1)	.951
Hypertension, n (%)	211 (39.3)	237 (50.6)	<.001*
Diabetes mellitus, n (%)	88 (16.4)	73 (15.6)	.745
Stroke or TIA, n (%)	84 (15.6)	64 (13.7)	.380
Vascular Disease, n (%)	74 (13.8)	69 (14.7)	.663
CHA ₂ DS ₂ -VASc score	1.8 ± 1.6	1.8 ± 1.5	.567
Echocardiography			
LA diameter, mm	42.1 ± 6.1	43.2 ± 6.3	.009*
LA volume index, mL/m ²	39.2 ± 13.3	40.7 ± 13.0	.077
LV ejection fraction, %	62.5 ± 8.3	61.9 ± 9.3	.271
E/Em	10.3 ± 4.6	10.4 ± 4.0	.865
LVEDD, mm	49.9 ± 4.8	50.2 ± 4.6	.264
LAA emptying velocity, cm/s	44.8 ± 21.7	43.1 ± 20.6	.314
CT/NavX (n = 976)			
LA volume/BSA, mL/m ²	87.7 ± 24.1	91.3 ± 26.0	.025*
Pericardial fat volume, cm ³	128.7 ± 58.9	128.9 ± 56.0	.956
LA endocardial voltage, mV	1.28 ± 0.64	1.04 ± 0.55	<.001*

Abbreviations: AF, atrial fibrillation; BMI, body mass index; BP, blood pressure; BSA, body surface area; CT, computed tomography; E/Em, early mitral inflow velocity over the early diastolic mitral annular velocity; LA, left atrium; LAA, left atrial appendage; LV, left ventricle; LVEDD, left ventricular end-diastolic dimension; TIA, transient ischemic attack.
*P < .05.

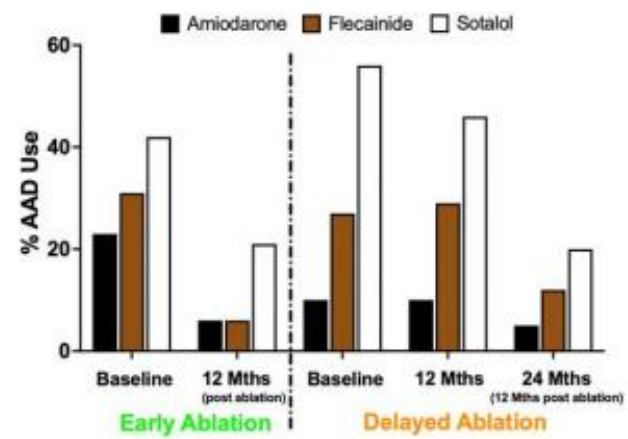
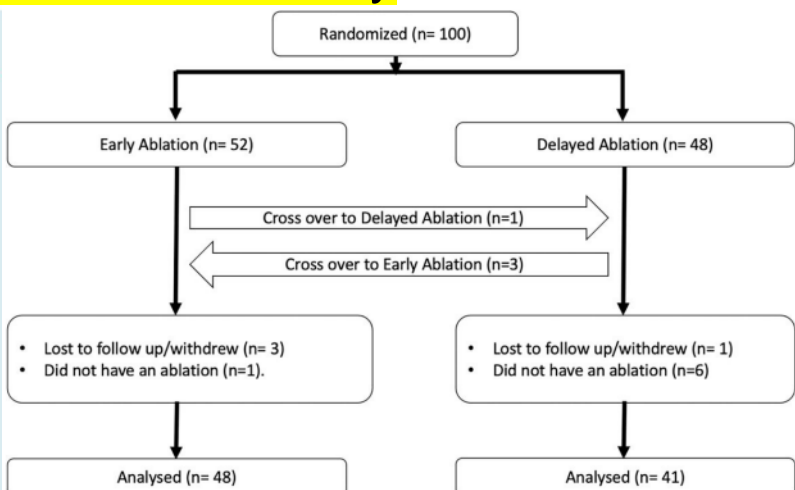


Background

- Compared with an early ablation strategy, **delaying AF ablation** by 12 months for AAD management **did not result in reduced ablation efficacy.**

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)
CHA ₂ DS ₂ -VASc score, mean ± SD	1.8 ± 1.6	1.2 ± 1.1
BMI, kg/m ² , mean ± SD	30 ± 5.5	30 ± 5.3
Hypertension, n (%)	26 (54)	22 (54)
Diabetes, n (%)	3 (6)	1 (2)
Heart failure, n (%)	6 (13)	2 (5)
Stroke/TIA, n (%)	3 (6)	0
Vascular disease, n (%)	13 (27)	6 (15)
OSA, n (%)	7 (15)	11 (27)
Regular alcohol intake, n (%)	6 (13)	8 (19)
eGFR, mL/min, mean (SD)	80 (13)	81 (11)
Anticoagulation, n (%)	43 (90)	34 (83)
Beta blockers, n (%)	18 (37)	11 (27)
CCB, n (%)	5 (10)	4 (10)
Digoxin, n (%)	7 (15)	2 (5)
AAD use, n (%)	46 (96)	38 (93)
Amiodarone, n (%)	11 (23)	4 (10)
Flecainide, n (%)	15 (31)	11 (26)
Sotalol, n (%)	20 (42)	23 (56)
AFSSS, median (Q1–Q3) ^a	14 (8–22)	15 (12–22)
LV ejection fraction, %, mean ± SD	57 ± 8	61 ± 5
E/E', mean ± SD	9.2 ± 4	9.1 ± 3
LA volume, mL/m ² , mean ± SD	45.5 ± 15	40.6 ± 11
LA size, cm, mean ± SD	4.7 ± 0.7	4.4 ± 0.7
LA area, cm ² , mean ± SD	28 ± 6	24 ± 5



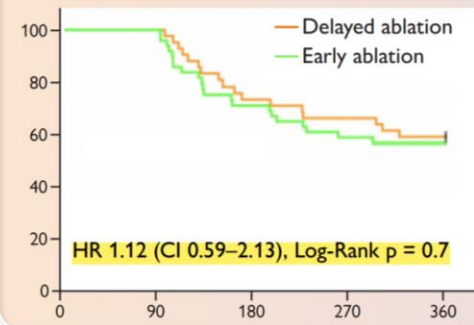
Design

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

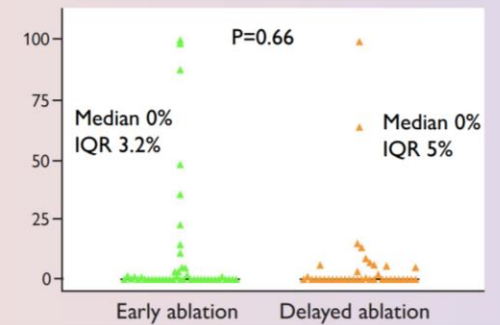
Endpoints

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

Arrhythmia-free survival at 12 months



Median AF burden at 12 months



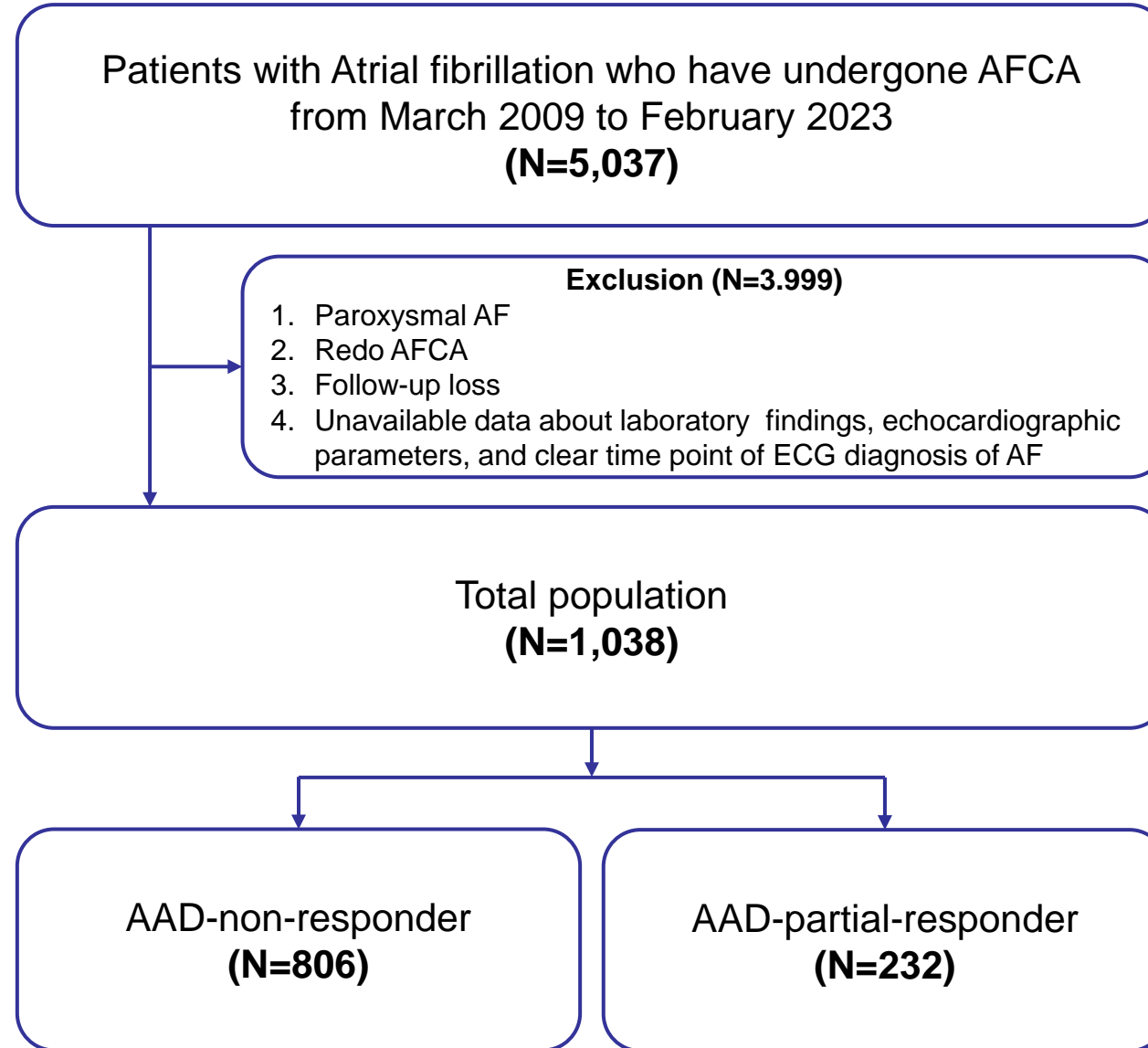
^aAFSSS: Range [0–35]. A higher score indicates the presence of physical symptoms of AF.

Aim of study

- This study aims to determine the relationship between the timing of AFCA and its late recurrence in patients with PeAF and elucidate the latest acceptable timing for AFCA.
- Additionally, we aim to elucidate the influence of Antiarrhythmic drugs (AAD) responsiveness on the relationship between AFCA timing and late recurrence.



Methods



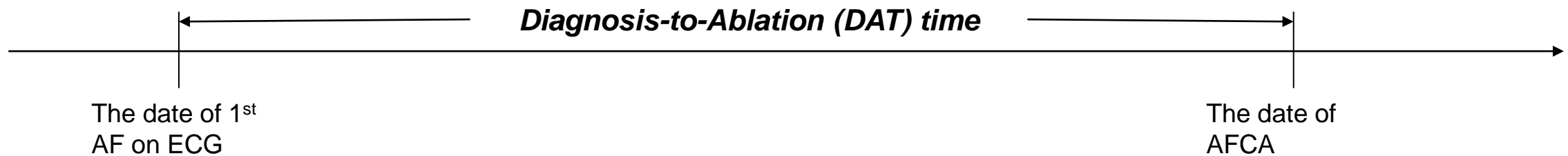
Flow chart of the study



Methods – Study definitions

- **Diagnosis-to-Ablation (DAT) time**

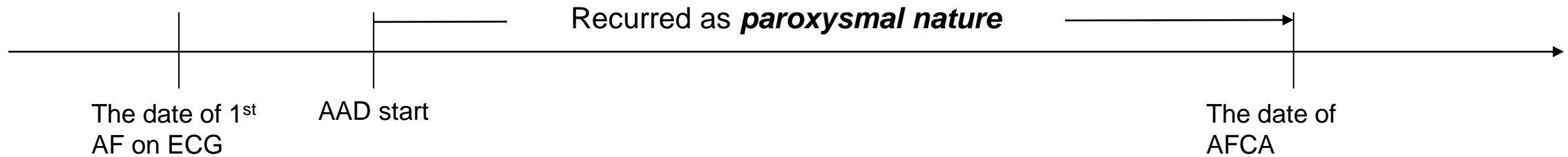
- the period from the day when AF was first diagnosed by electrocardiogram (ECG) to the day when the AFCA procedure was performed



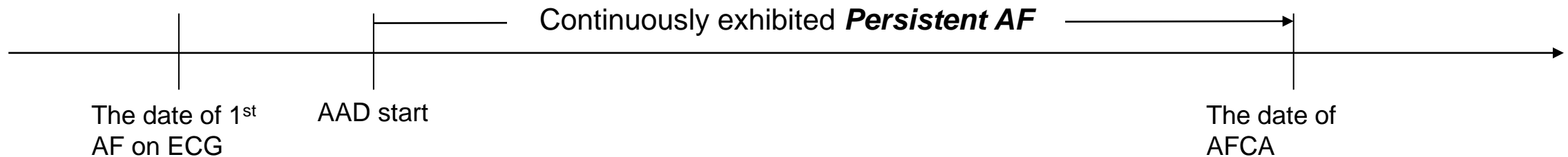
Methods – Study definitions

- **AAD responsiveness**

- *AAD-partial-responder*



- *AAD-non-responder*



Methods – Study definitions

- **Primary outcome**
 - the duration of free from recurrence of atrial arrhythmia (AF, atrial tachycardia, or AFL) lasting for 30 seconds or more beyond the 90-day blanking period.



Result – Baseline characteristics between AAD-partial-responder and non-responder

	AAD-non-responder (N=806)	AAD-partial-responder (N=232)	p-value
Age, y	61.0 [54.0;68.0]	62.0 [55.0;68.5]	0.194
Male sex, n (%)	662 (82.1%)	166 (71.6%)	0.001
BMI, kg/m ²	25.3 [23.5;27.4]	24.9 [22.8;26.6]	0.007
BSA	1.9 [1.8; 2.0]	1.8 [1.7; 1.9]	<0.001
Comorbidities			
Congestive heart failure, n (%)	202 (25.1%)	59 (25.4%)	0.977
Hypertension, n (%)	420 (52.1%)	118 (50.9%)	0.795
Diabetes mellitus, n (%)	149 (18.5%)	39 (16.8%)	0.626
Stroke or TIA, n (%)	104 (12.9%)	35 (15.1%)	0.453
Vascular disease, n (%)	57 (7.1%)	23 (9.9%)	0.197
CHA ₂ DS ₂ -VASc score	2.0 [1.0; 3.0]	2.0 [1.0; 3.0]	0.181
Echocardiography			
LA diameter, mm	44.0 [41.0;48.0]	41.0 [37.0;46.0]	<0.001
LA volume index, mL/m ²	43.0 [36.4;52.9]	38.0 [31.6;45.9]	<0.001
LV ejection fraction, %	62.0 [57.0;67.0]	63.0 [59.0;68.0]	0.004
E/E'	9.1 [7.4;11.7]	9.3 [7.8;12.4]	0.140
E velocity, m/s	0.8 [0.7; 0.9]	0.7 [0.6; 0.8]	<0.001
Peak TR velocity, m/s	2.3 [2.1; 2.5]	2.3 [2.1; 2.5]	0.352
RVSP, mmHg	26.0 [23.0;31.0]	25.0 [22.0;30.0]	0.169



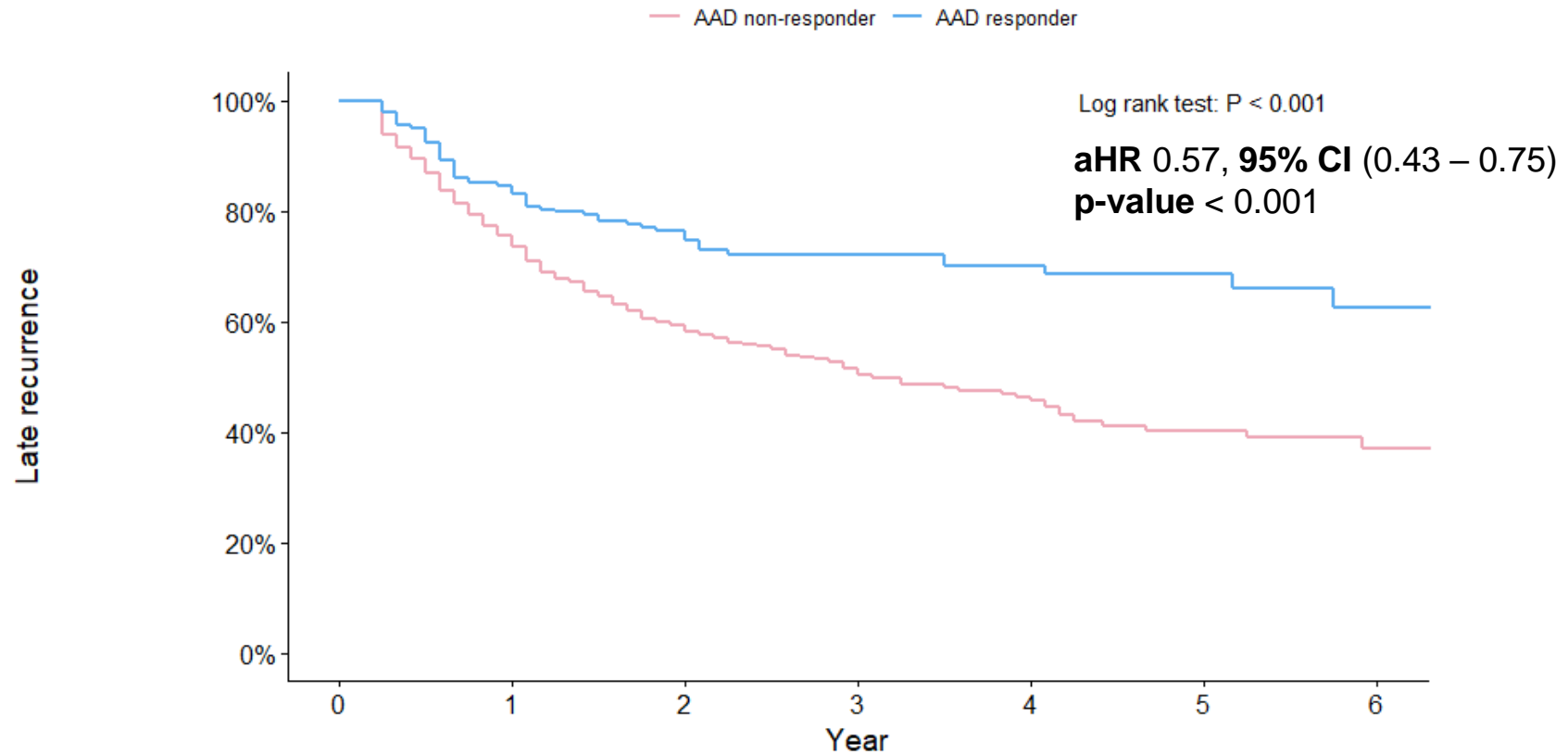
Result – Baseline characteristics between AAD-partial-responder and non-responder

	AAD-non-responder (N=806)	AAD-partial-responder (N=232)	p-value
Laboratory findings			
BUN	16.5 [14.0;19.8]	15.6 [13.1;18.4]	0.001
Creatinine	1.0 [0.8; 1.1]	0.9 [0.8; 1.0]	<0.001
Serum albumin	4.4 [4.2; 4.6]	4.4 [4.1; 4.6]	0.014
GFR	77.0 [68.0;86.0]	80.0 [67.5;93.0]	0.039
Hb	14.9 [14.0;15.8]	14.2 [13.2;15.4]	0.000
RDW	12.8 [12.3;13.3]	12.8 [12.4;13.3]	0.990
Lymphocyte count	2.0 [1.7; 2.6]	2.0 [1.7; 2.5]	0.940
Total cholesterol	169.0 [138.0;196.0]	164.0 [138.0;187.5]	0.261
HDL-cholesterol	46.0 [40.5;53.0]	48.0 [41.0;54.8]	0.199
LDL-cholesterol	97.5 [71.5;122.0]	91.0 [68.0;116.5]	0.103
Triglycerides	114.0 [83.2;158.0]	108.2 [79.0;155.7]	0.218
Serum glucose	102.0 [94.5;113.2]	102.5 [95.4;111.6]	0.979
HbA1c	6.4 [6.0; 6.9]	6.2 [5.9; 7.0]	0.392
Pericardial fat volume			
Total PFV, cm ³	123.4 [96.4;156.3]	105.8 [77.3;136.5]	<0.001
Atrial PFV, cm ³	52.1 [39.7;68.2]	42.9 [30.8;56.3]	<0.001
Ventricular PFV, cm ³	70.1 [53.2;88.5]	61.7 [45.9;79.7]	<0.001



Result

Late recurrence after AFCA



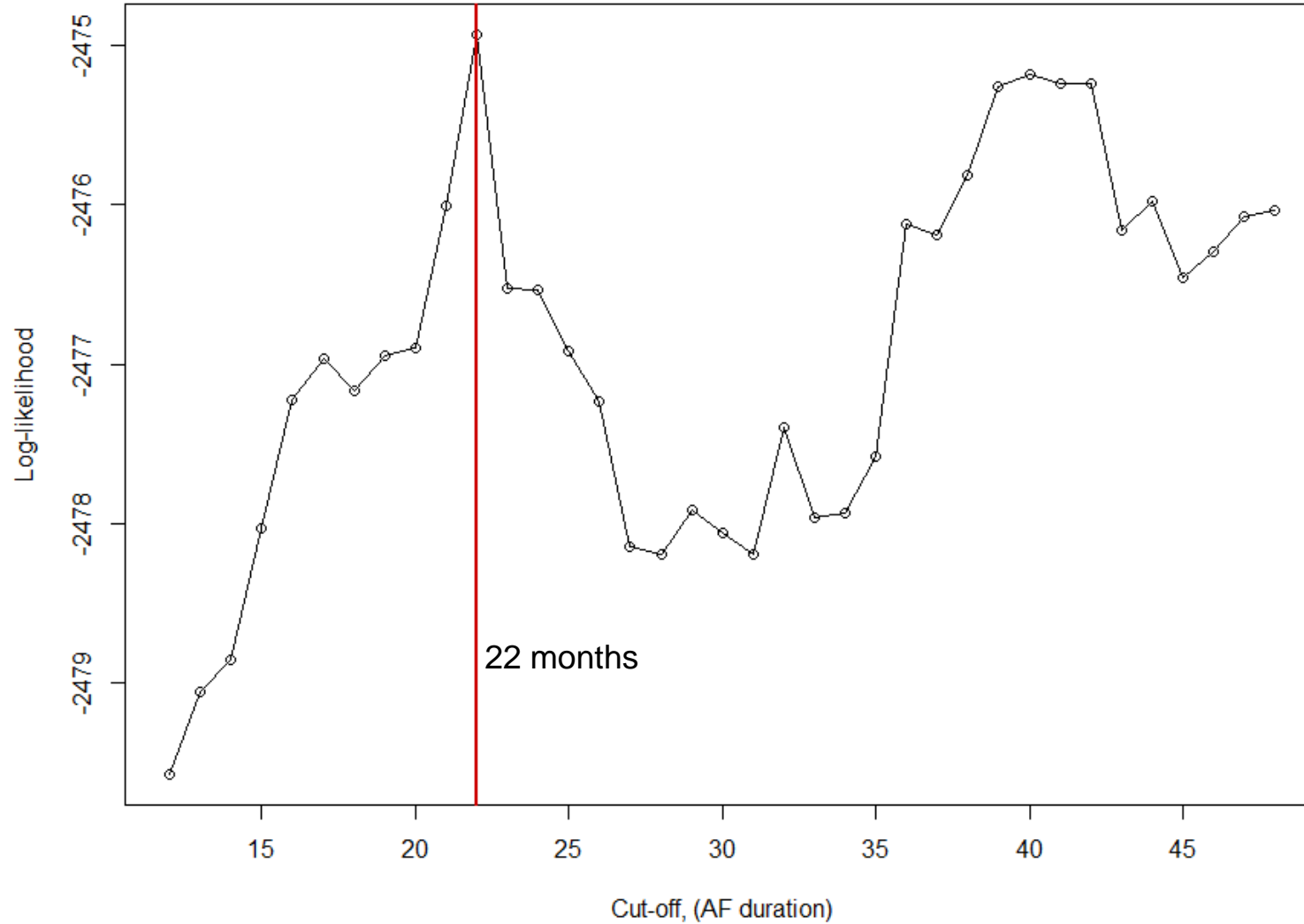
Number at risk

AAD non-responder	804	512	268	131	75	37	18
AAD responder	232	176	126	82	51	30	17



Result

Log-likelihood graph of Cox regression model of late recurrence after AFCA in patients with PeAF



Result – Baseline characteristics between DAT ≤ 22 months and DAT > 22 months

	DAT ≤ 22 months (N=470)	DAT > 22 months (N=568)	p-value
Age, y	60.0 [53.0;67.0]	61.0 [55.0;68.0]	0.151
Male sex, n (%)	376 (80.0%)	452 (79.6%)	0.927
BMI, kg/m ²	25.1 [23.2;27.4]	25.3 [23.5;27.1]	0.902
BSA	1.9 [1.7; 2.0]	1.9 [1.7; 2.0]	0.885
Comorbidities			
Congestive heart failure, n (%)	112 (23.8%)	149 (26.2%)	0.414
Hypertension, n (%)	260 (55.3%)	278 (48.9%)	0.047
Diabetes mellitus, n (%)	88 (18.7%)	100 (17.6%)	0.701
Stroke or TIA, n (%)	68 (14.5%)	71 (12.5%)	0.404
Vascular disease, n (%)	41 (8.7%)	39 (6.9%)	0.317
CHA ₂ DS ₂ -VASc score	2.0 [1.0; 3.0]	2.0 [1.0; 3.0]	0.227
Echocardiography			
LA diameter, mm	43.0 [40.0;47.0]	44.0 [40.0;48.0]	0.080
LA volume index, mL/m ²	41.2 [34.9;51.0]	42.2 [35.5;51.2]	0.239
LV ejection fraction, %	62.0 [57.0;67.0]	62.0 [58.0;67.0]	0.036
E/E'	9.1 [7.7;11.4]	9.2 [7.4;12.2]	0.342
E velocity, m/s	0.8 [0.6; 0.9]	0.8 [0.7; 0.9]	0.393
Peak TR velocity, m/s	2.3 [2.1; 2.5]	2.3 [2.1; 2.5]	0.359
RVSP, mmHg	26.0 [22.0;30.0]	26.0 [23.0;31.0]	0.395



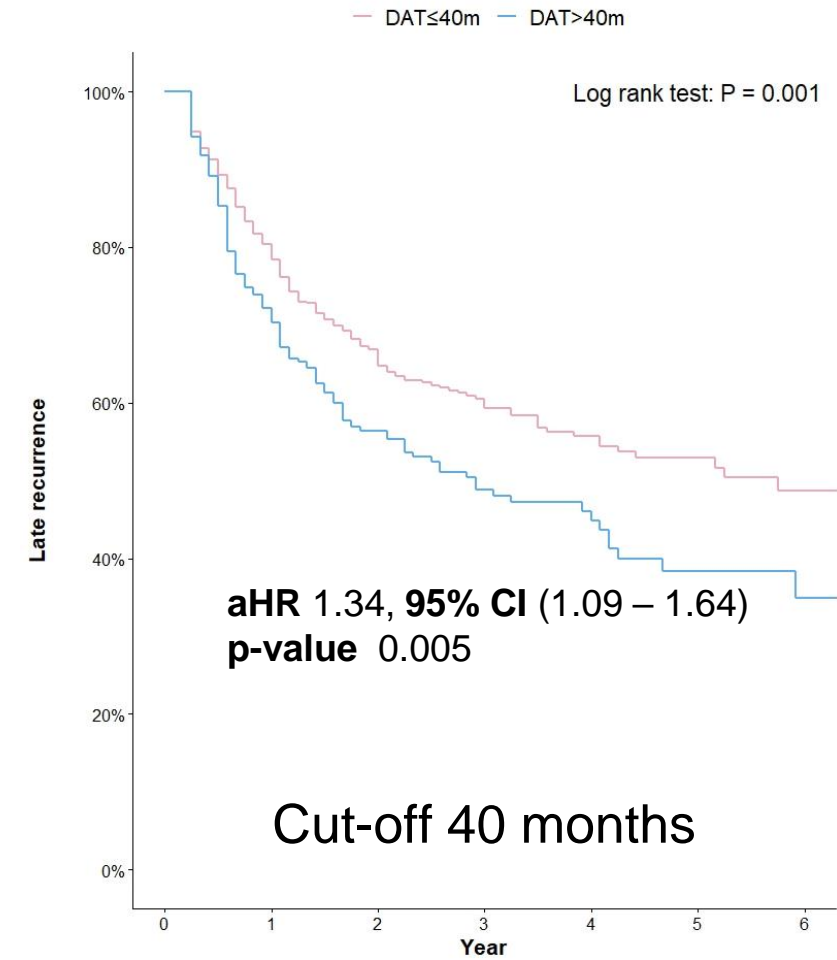
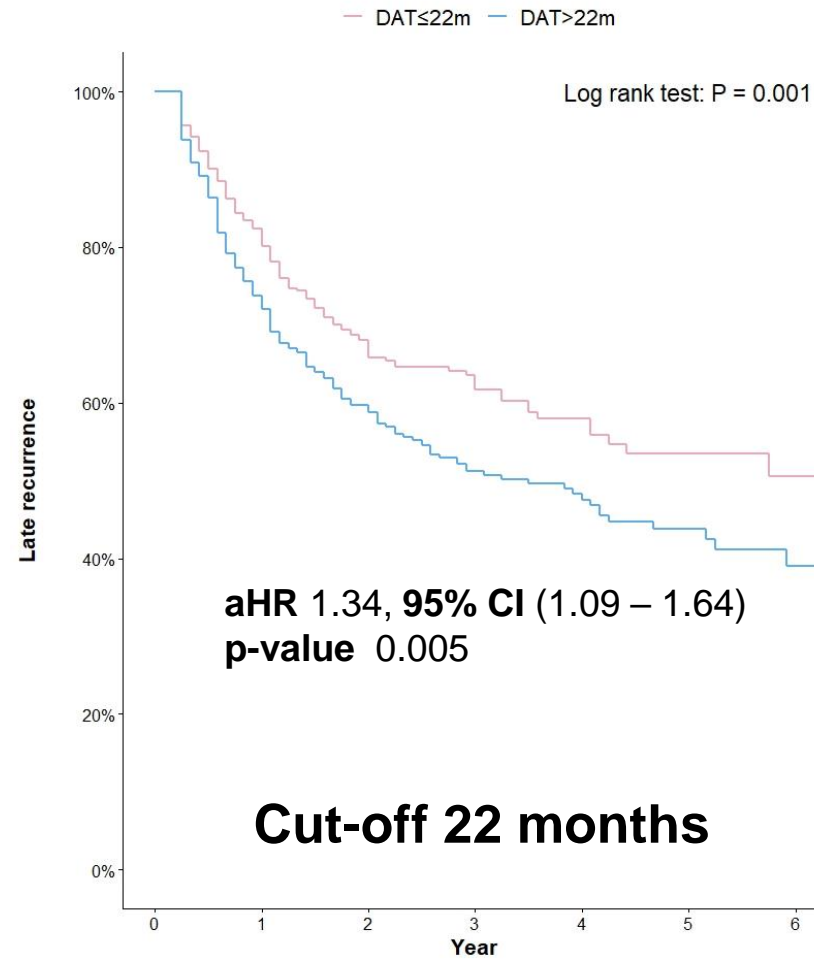
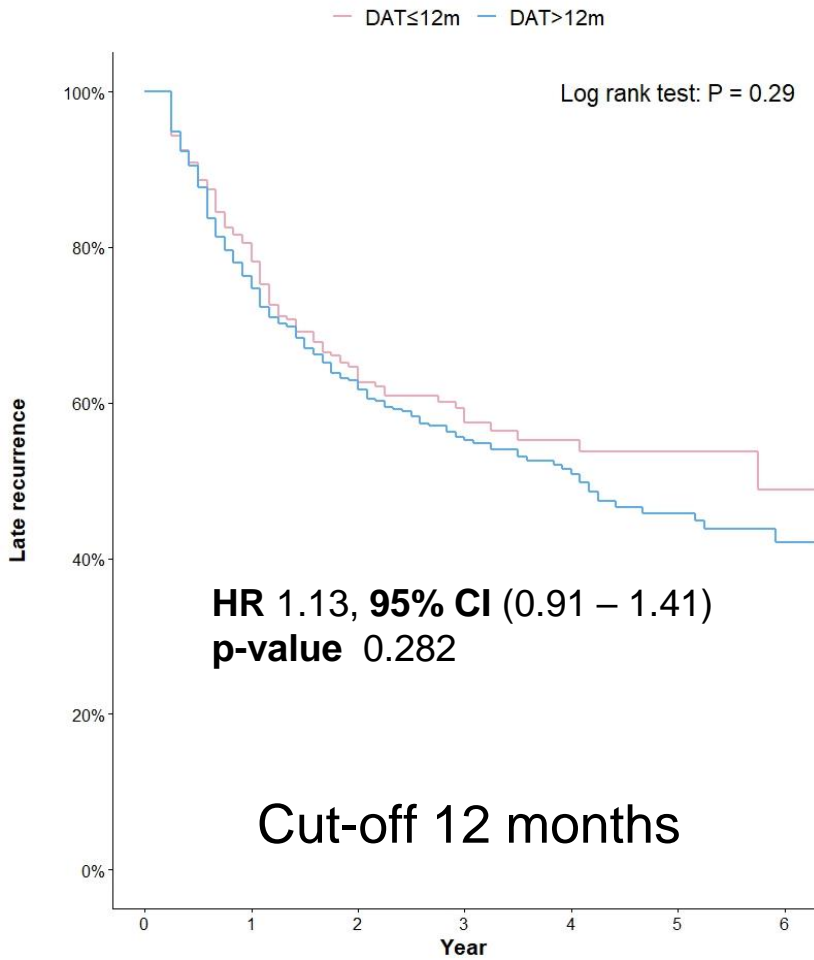
Result – Baseline characteristics between DAT ≤ 22 months and DAT > 22 months

	DAT ≤ 22 months (N=470)	DAT > 22 months (N=568)	p-value
Laboratory findings			
BUN	16.4 [13.8;19.4]	16.4 [13.9;19.5]	0.976
Creatinine	1.0 [0.8; 1.1]	1.0 [0.8; 1.1]	0.696
Serum albumin	4.4 [4.2; 4.6]	4.4 [4.2; 4.6]	0.954
GFR	78.0 [68.0;88.0]	77.0 [68.0;86.5]	0.323
Hb	14.7 [13.6;15.8]	14.9 [13.9;15.8]	0.172
RDW	12.8 [12.3;13.2]	12.9 [12.4;13.3]	0.288
Lymphocyte count	2.0 [1.7; 2.6]	2.1 [1.7; 2.5]	0.648
Total cholesterol	164.0 [135.0;195.0]	168.0 [141.0;193.0]	0.469
HDL-cholesterol	46.0 [39.8;53.0]	47.0 [42.0;54.0]	0.038
LDL-cholesterol	93.0 [66.5;122.2]	97.0 [72.7;120.8]	0.311
Triglycerides	115.5 [84.0;164.0]	109.0 [81.0;151.0]	0.092
Serum glucose	103.0 [95.0;114.0]	101.5 [94.0;111.0]	0.067
HbA1c	6.2 [6.0; 7.0]	6.3 [5.9; 6.9]	0.960
Pericardial fat volume			
Total PFV, cm ³	117.3 [90.4;150.4]	121.9 [91.6;154.6]	0.351
Atrial PFV, cm ³	50.2 [37.1;63.6]	50.6 [38.0;67.1]	0.378
Ventricular PFV, cm ³	68.6 [51.7;86.2]	68.8 [51.2;87.7]	0.433



Result

Survival analyses by cut-off value for DAT



Number at risk

	0	1	2	3	4	5	6
DAT ≤ 12m	336	230	128	67	36	19	10
DAT > 12m	700	458	266	146	90	48	25

Number at risk

	0	1	2	3	4	5	6
DAT ≤ 22m	469	330	189	105	56	29	18
DAT > 22m	567	358	205	108	70	38	17

Number at risk

	0	1	2	3	4	5	6
DAT ≤ 40m	701	482	279	150	87	46	26
DAT > 40m	335	206	115	63	39	21	9

Discussion

- The major findings in our study are as follows:
 1. In AAD-partial-responders, the incidence of late recurrence after AFCA was lower than AAD-non-responders.
 2. In patients with PeAF, we were able to confirm a significant difference in the risk of late recurrence after AFCA, with a cut-off value of 22 months for DAT estimated through MLE.
 3. These results suggest that in patients with PeAF, the implementation of AFCA should not be postponed until after 22 months of DAT.



Limitations

- We evaluated a single-center cohort retrospectively
- Even DAT cannot accurately reflect the disease progression period of AF
- There were several differences in baseline characteristics between the groups in the comparison based on AAD responsiveness.



Conclusion

- Both DAT and AAD responsiveness affected rhythm control outcome of AFCA in patients with PeAF.
- Delaying AFCA longer than 22 months of DAT is not desirable in patients with PeAF even under optimal medical therapy with AADs



Thank you for your attention!

