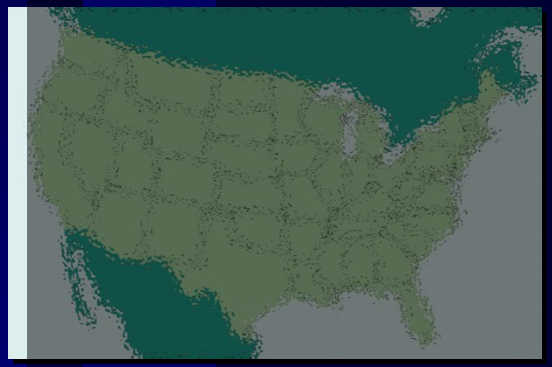


Rate vs Rhythm Post Cabana: Living On A Prayer

Andrea Natale MD

Executive Medical Director, Texas Cardiac Arrhythmia Institute,

St. David's Medical Center, Austin, Texas

Professor of Medicine, Dell Medical School, Austin, Texas

Director of Interventional EP, Scripps Green, San Diego, CA

Clinical Professor, Case Western Reserve University, Cleveland, Ohio

Consulting Professor, Stanford University, Palo Alto, California

DILEMMMA!!!

RATE CONTROL
VS
RHYTHM CONTROL

Atrial Fibrillation

?

Rate Control

Rhythm Control

Atrial Fibrillation Patients on Drugs

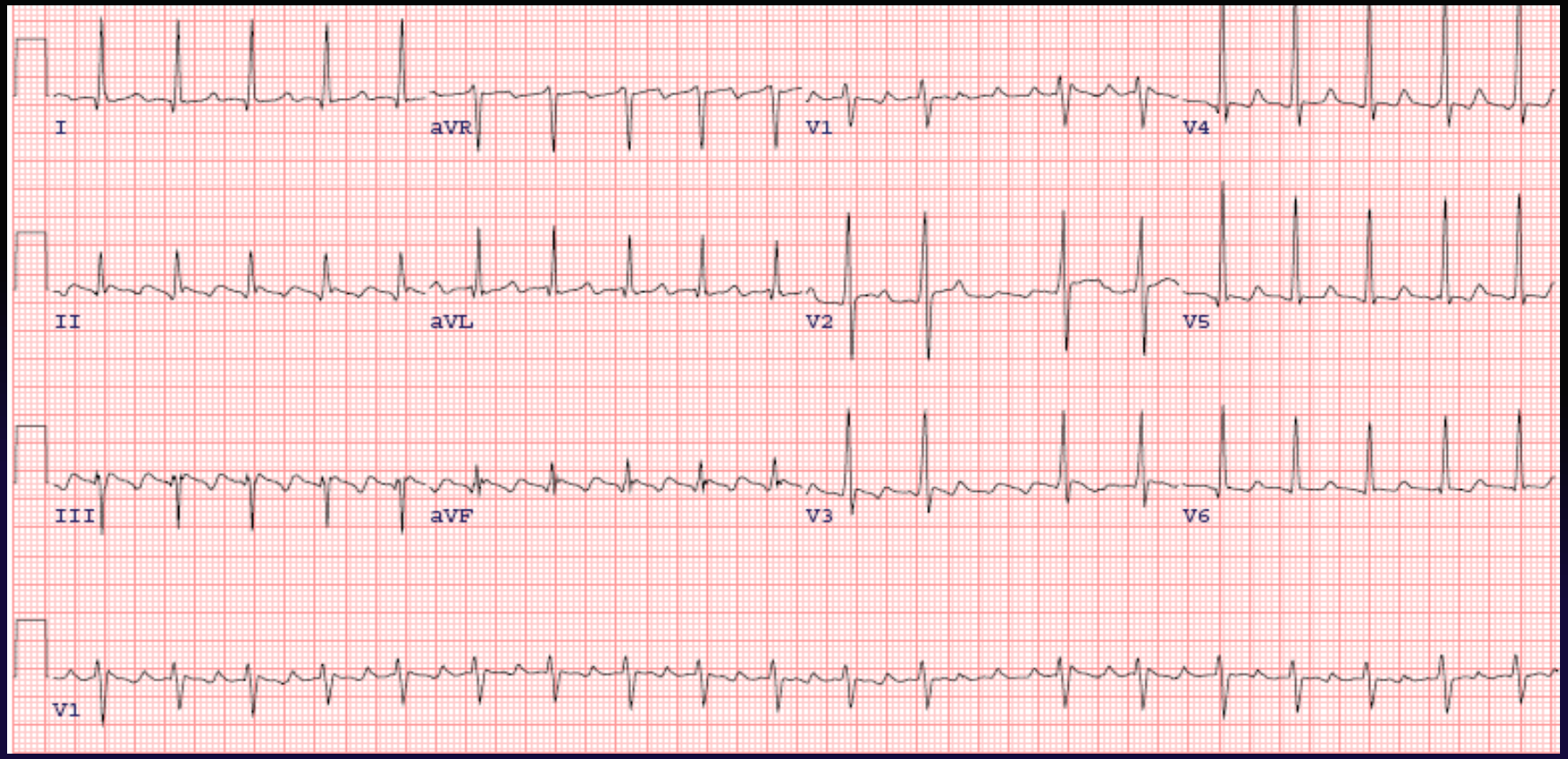
…After Catheter Ablation

Misdiagnosis of A. fibrillation as A.flutter

- Distinction is critical:
  - AFl:
    - ablation essentially 100% effective
    - type I AADs proarrhythmic
  - AFib:
    - ablation successful 70-75% (paroxysmal)
    - type I AADs can be helpful
- AF and AFl can coexist
- ECG characteristics are important

- organized in V1 (not other leads, common mistake tele)
- irregular ventricular response
- no relationship between “flutter waves” and QRS

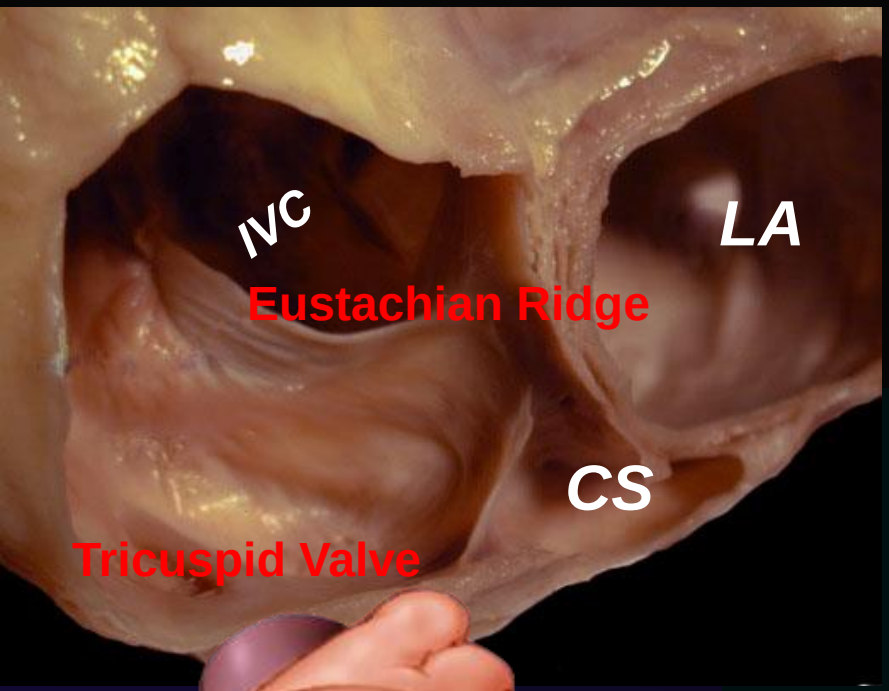
Atrial flutter

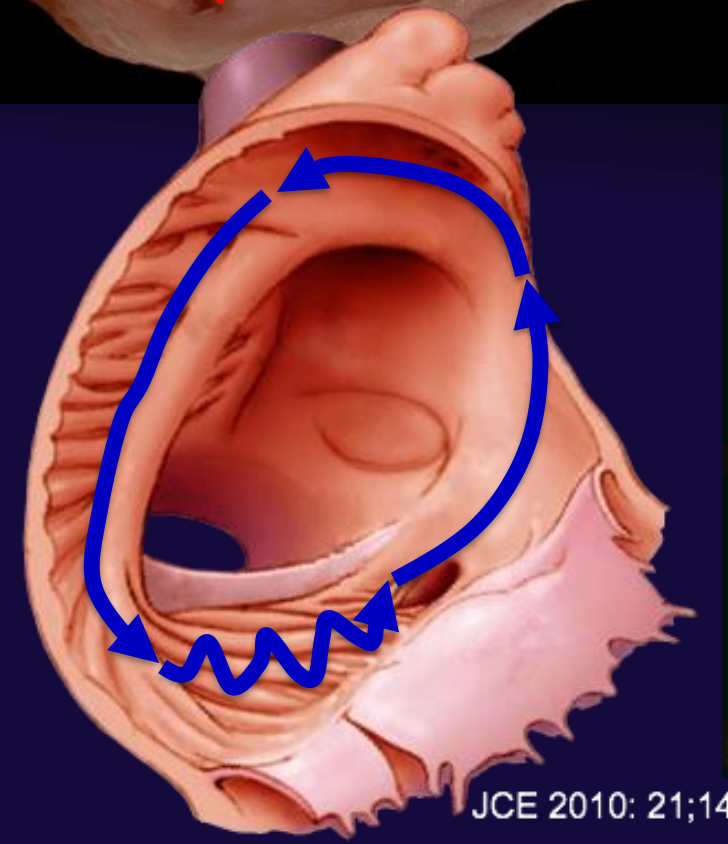


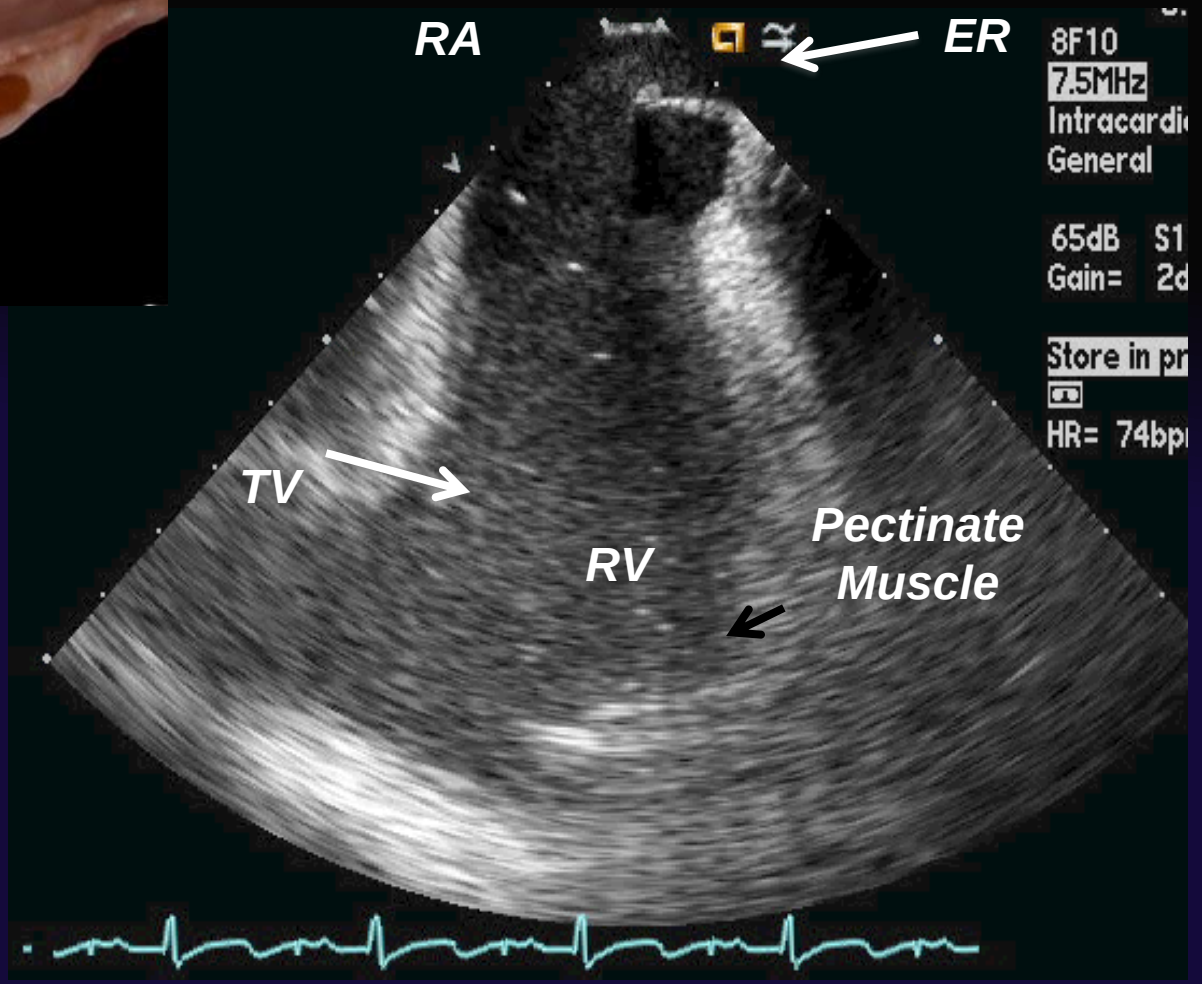
- flutter waves consistent in all leads
- opposite polarity of inferior leads and V1
- ventricular response regular (2:1, 4:1)

RA Anatomy-

Cavo Tricuspid Isthmus







JCE 2010: 21;144-149

You consider continuing coumadin:

1. No coumadin since no risk of other atrial arrhythmias
2. Low risk of atrial arrhytmias, so will start ASA
3. Afib risk at follow up is between 30-50%, so will consider coumadin based on CHADS2 score

You consider continuing coumadin:

1. No coumadin since no risk of other atrial arrhythmias
2. Low risk of atrial arrhytmias, so will start ASA
3. Afib risk at follow up is between 50-80%, so will consider coumadin based on CHADS2 score

Incidence of Atrial Fibrillation Post-Cavotricuspid Isthmus Ablation in Patients with Typical Atrial Flutter: Left-Atrial Size as an Independent Predictor of Atrial Fibrillation Recurrence

KEITH ELLIS, M.D., OUSSAMA WAZNI, M.D., NASSIR MARROUCHE, M.D., DAVID MARTIN, M.D., MARC GILLINOV, M.D., PATRICK MCCARTHY, M.D., EDUARDO B. SAAD, M.D., MANDEEP BHARGAVA, M.D., ROBERT SCHWEIKERT, M.D., WALID SALIBA, M.D., DIANNA BASH, R.N., ANTONIO ROSSILLO, DEMET ERCIYES, PATRICK TCHOU, M.D., and ANDREA NATALE, M.D.

(J Cardiovasc Electrophysiol, Vol. 18, pp. 799-802, August 2007)

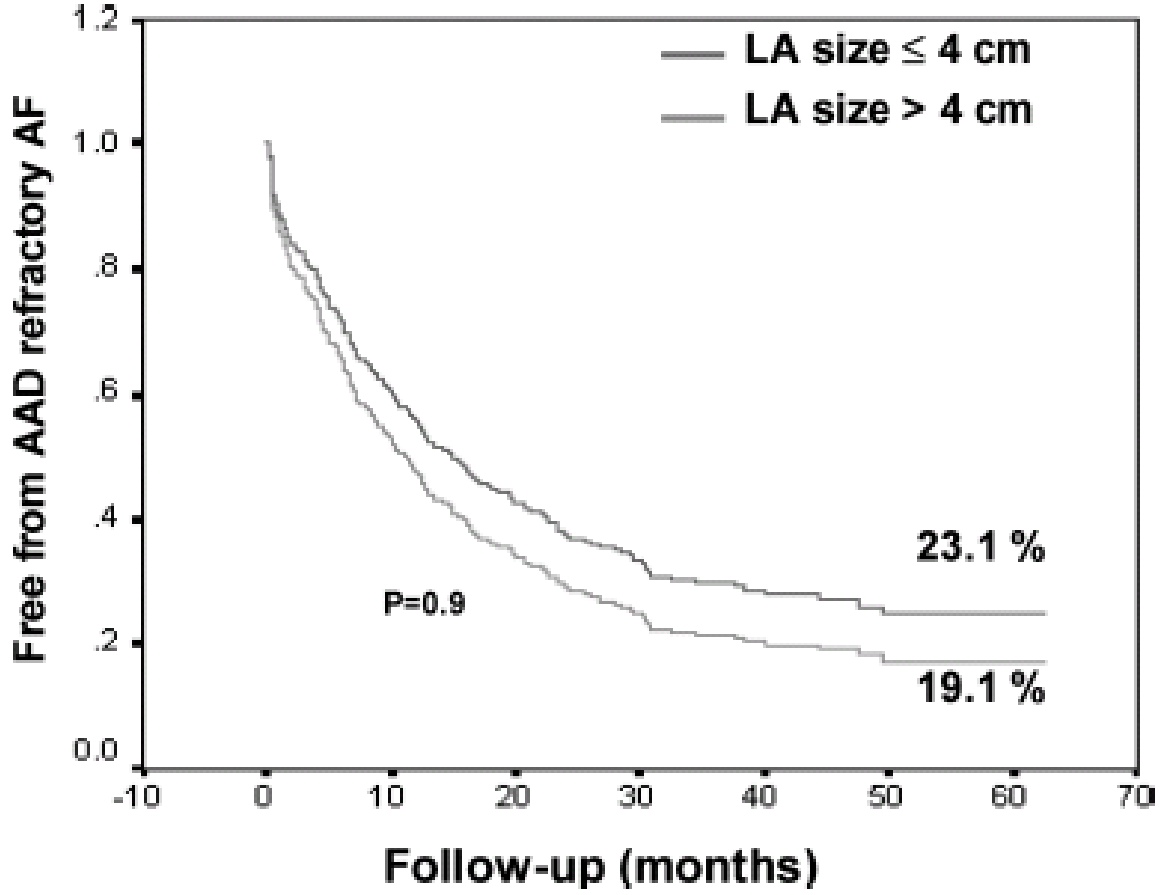


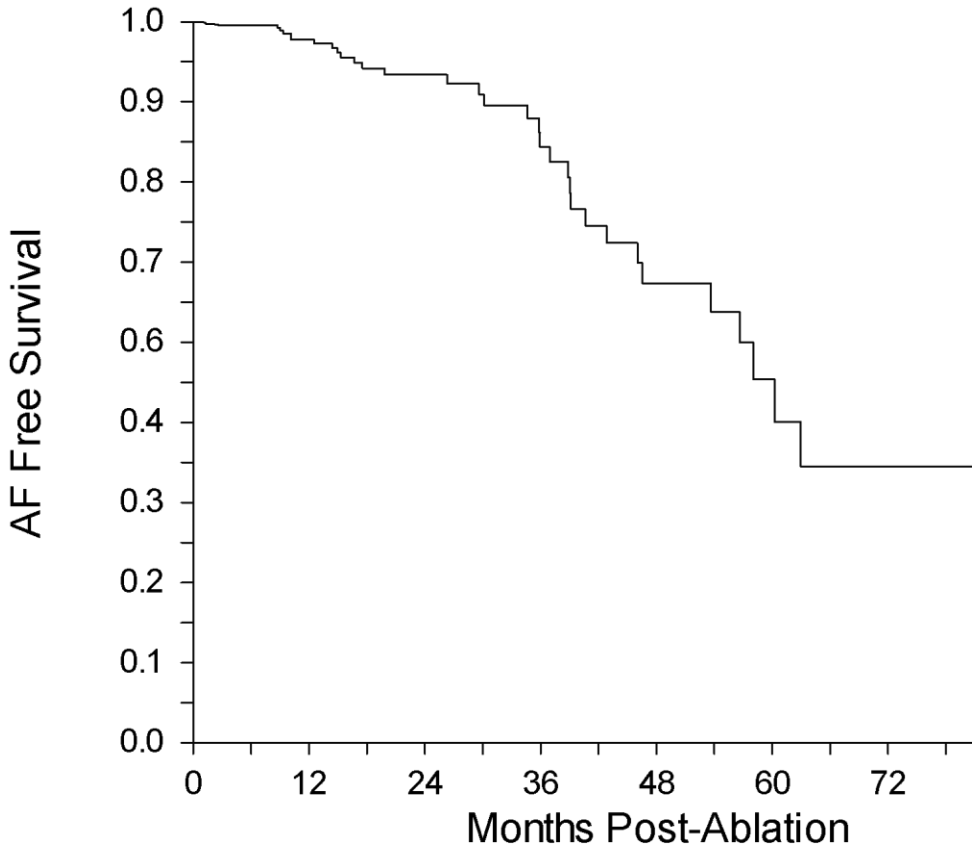
Figure 1. *Left-atrial size as a predictor of atrial fibrillation-free interval.*

Atrial fibrillation is common after ablation of isolated atrial flutter during long-term follow-up

Jason S. Chinitz, MD, Edward P. Gerstenfeld, MD, Francis E. Marchlinski, MD, David J. Callans, MD

(Heart Rhythm 2007;4:1029 –1033)

Incidence of AF in long term FU



80 patients with isolated isthmus dependent atrial flutter

50% incidence of AF after mean follow up of 30 months

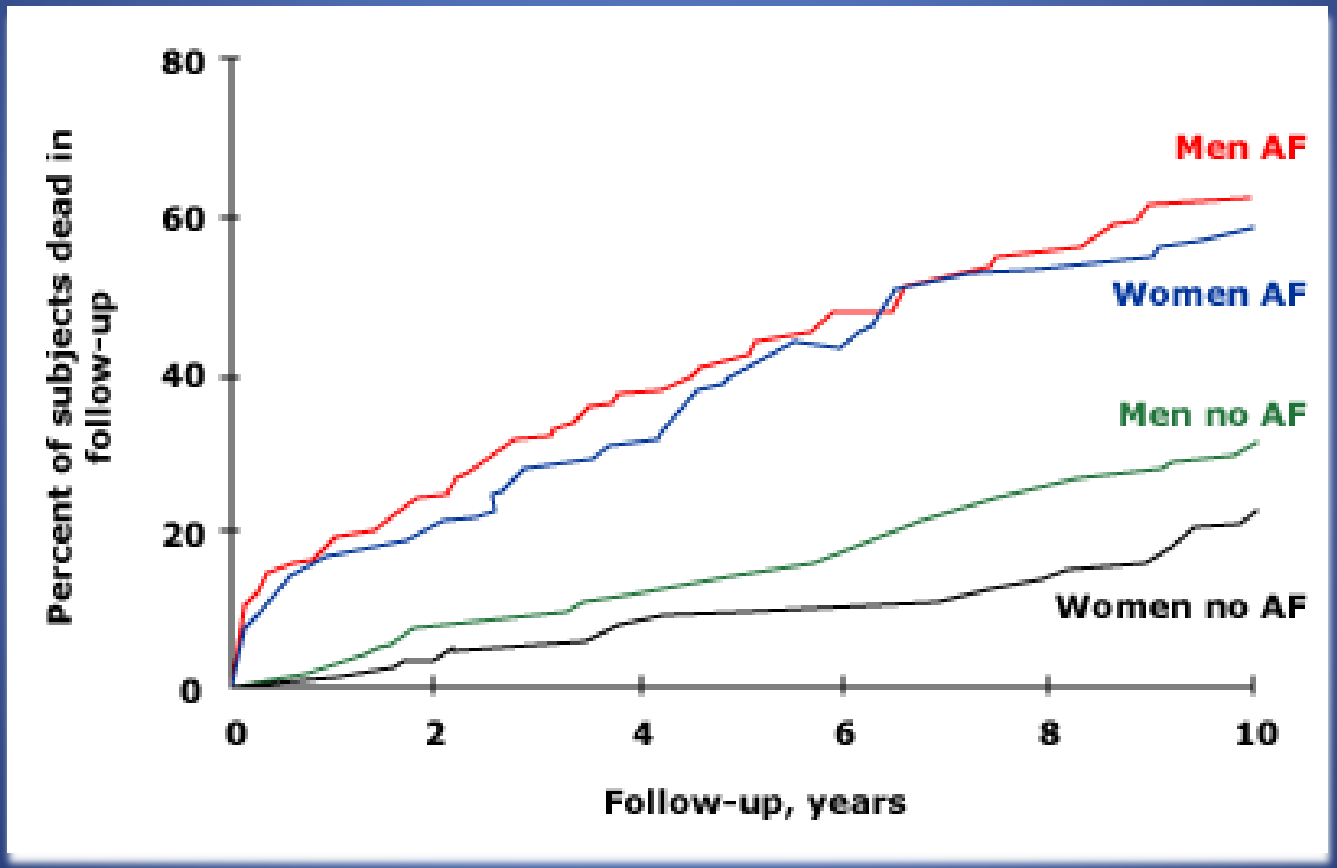
Chinitz J: Heart Rhythm 2007

Putting AF into Context…….

Impact of Atrial Fibrillation on the Risk of Death

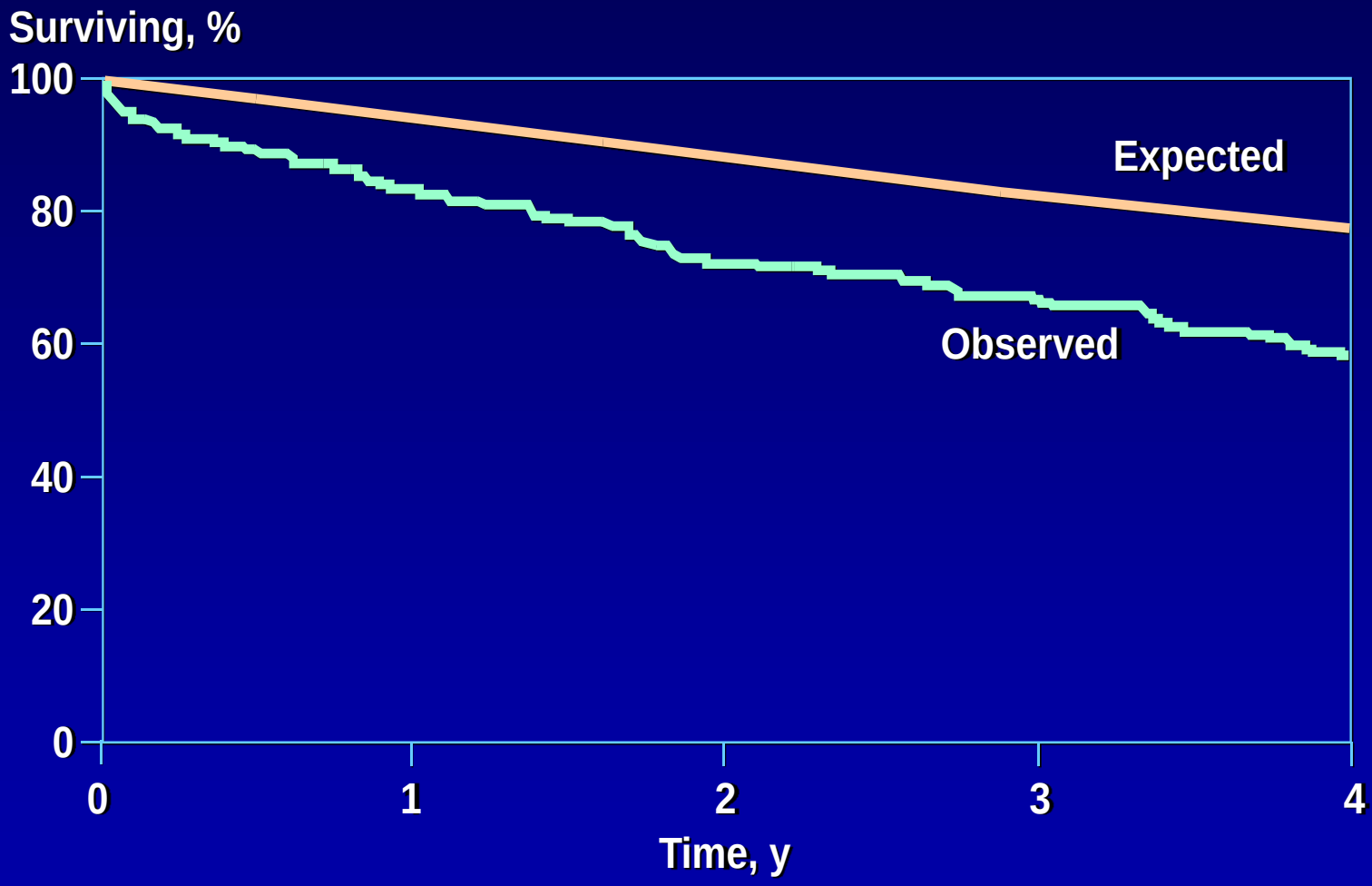
The Framingham Heart Study

Emelia J. Benjamin, MD, ScM; Philip A. Wolf, MD; Ralph B. D'Agostino, PhD; Halit Silbershatz, PhD; William B. Kannel, MD; Daniel Levy, MD



Circulation. 1998

Observed vs Expected Survival in Patients from Date of Onset of AF to Death or Follow-up: The Olmsted County Study



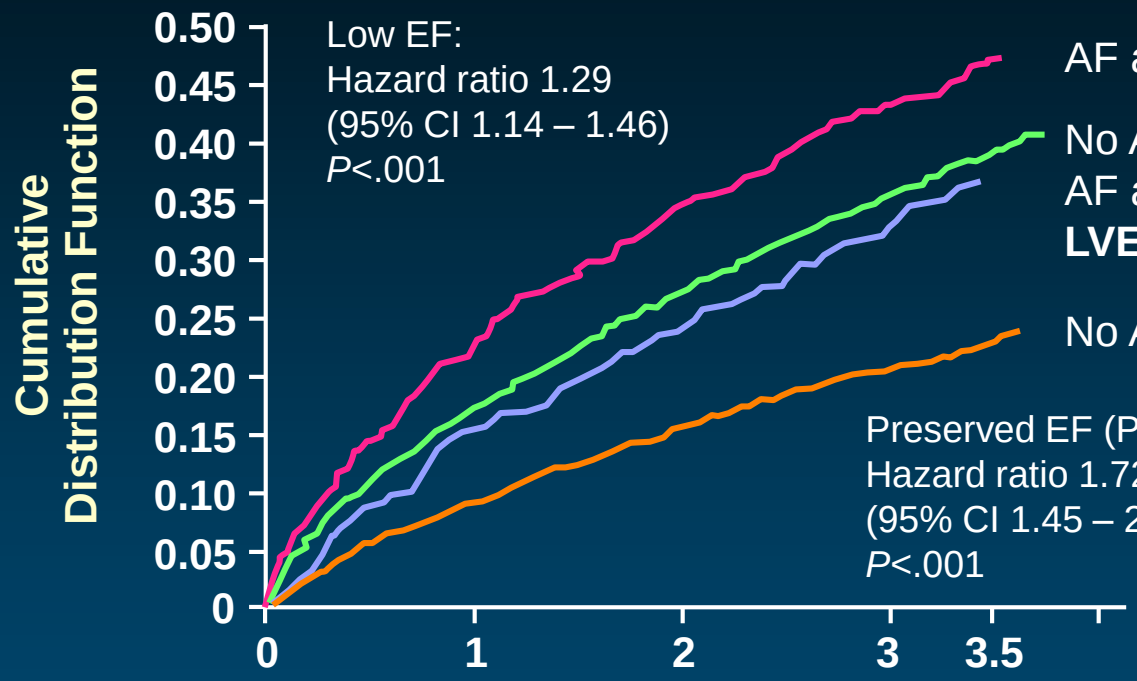
Keating et al. Am J Cardiol 2005;96:1420-1424

Atrial Fibrillation: Risk of Increased Mortality AVID Registry

- 3762 patients
- Mean follow up: 773 ± 420 days
- 24.4 % had history of AF
- AF was an independent predictor of mortality (relative risk = 1.20, 95% C.I. = 1.03 – 1.40)

AF Is a Marker for Worse Outcomes in Heart Failure: CHARM Program

Time to cardiovascular death or heart failure hospitalization

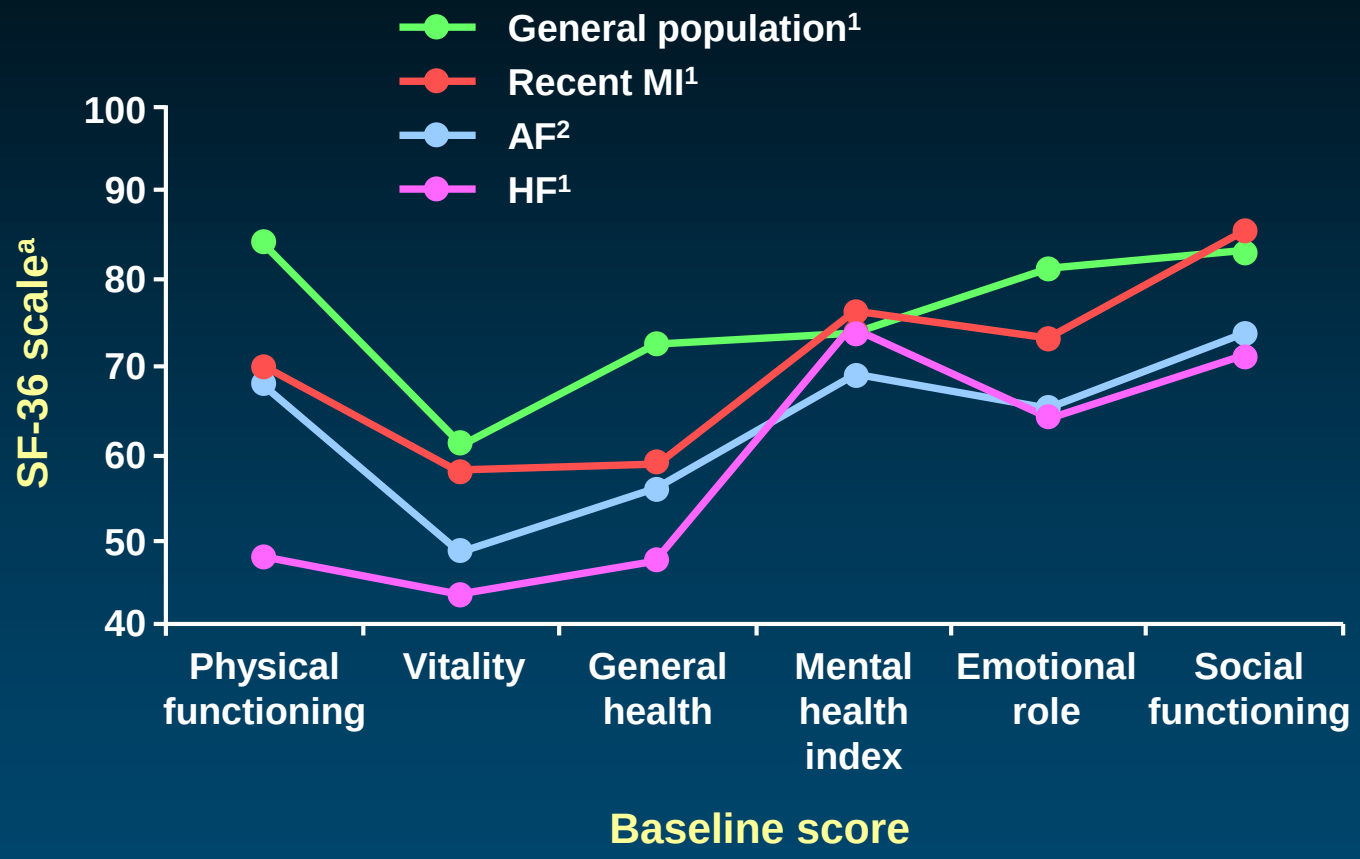


Number at risk				
No AF & Low EF	3906	3207	2755	1963
No AF & PEF	2545	2294	2096	1276
AF & Low EF	670	509	417	289
AF & PEF	478	399	353	203

AF predicted mortality for both preserved EF and depressed EF groups, and CV death or heart failure hospitalizations for preserved EF group

Reproduced with permission from Olsson LG, et al. *J Am Coll Cardiol.* 2006;47(10):1997-2004.

Impact on QoL: AF vs Other CV Illness

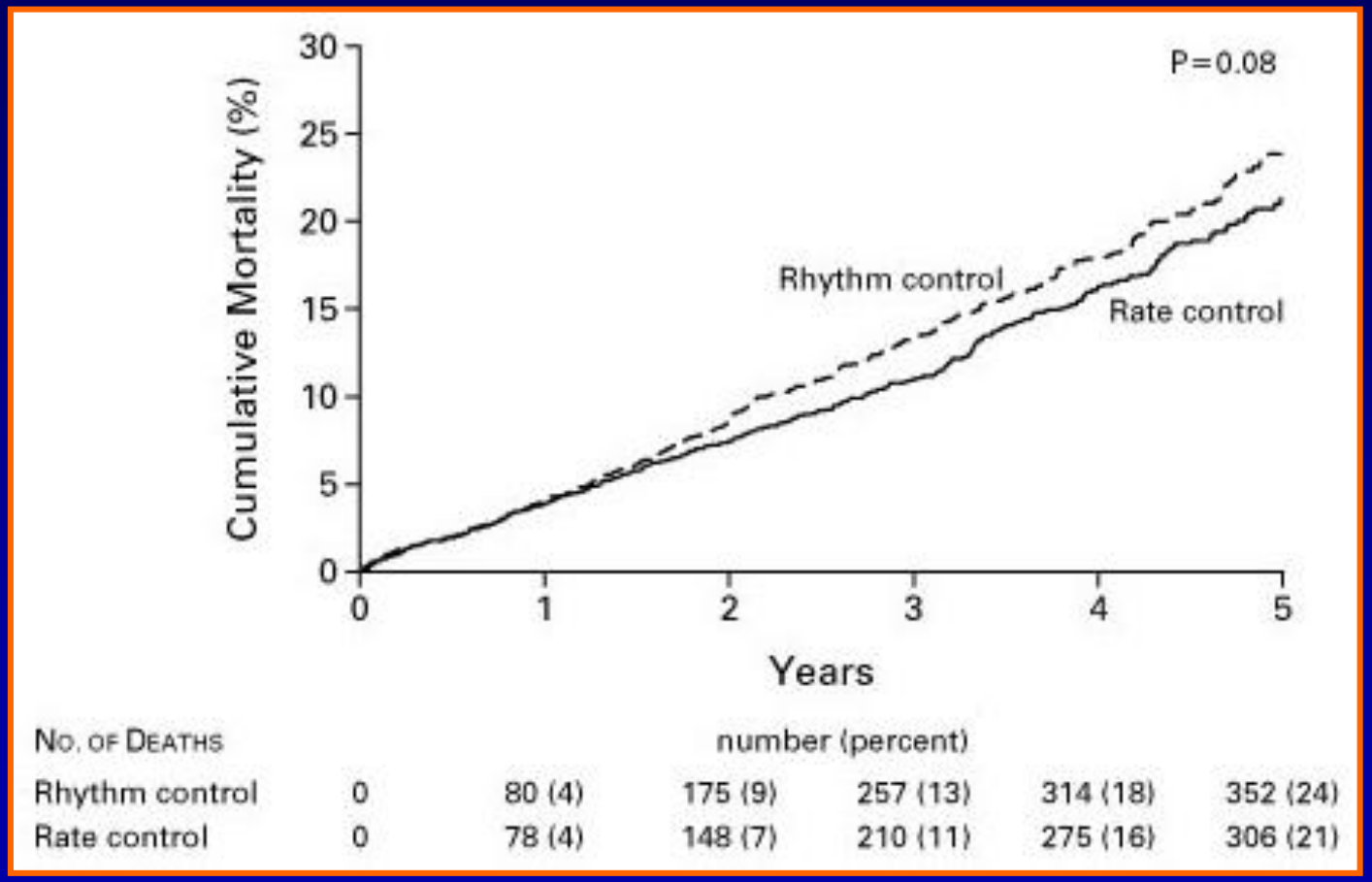


[a]Higher numbers indicate higher QoL.
SF-36 = Medical Outcomes Study Short Form 36.

1. Ware JE, et al. New England Medical Center Health Survey; 1993.
2. Dorian P, et al. *J Am Coll Cardiol*. 2000;36(3):1303-1309.

A COMPARISON OF RATE CONTROL AND RHYTHM CONTROL IN PATIENTS WITH ATRIAL FIBRILLATION

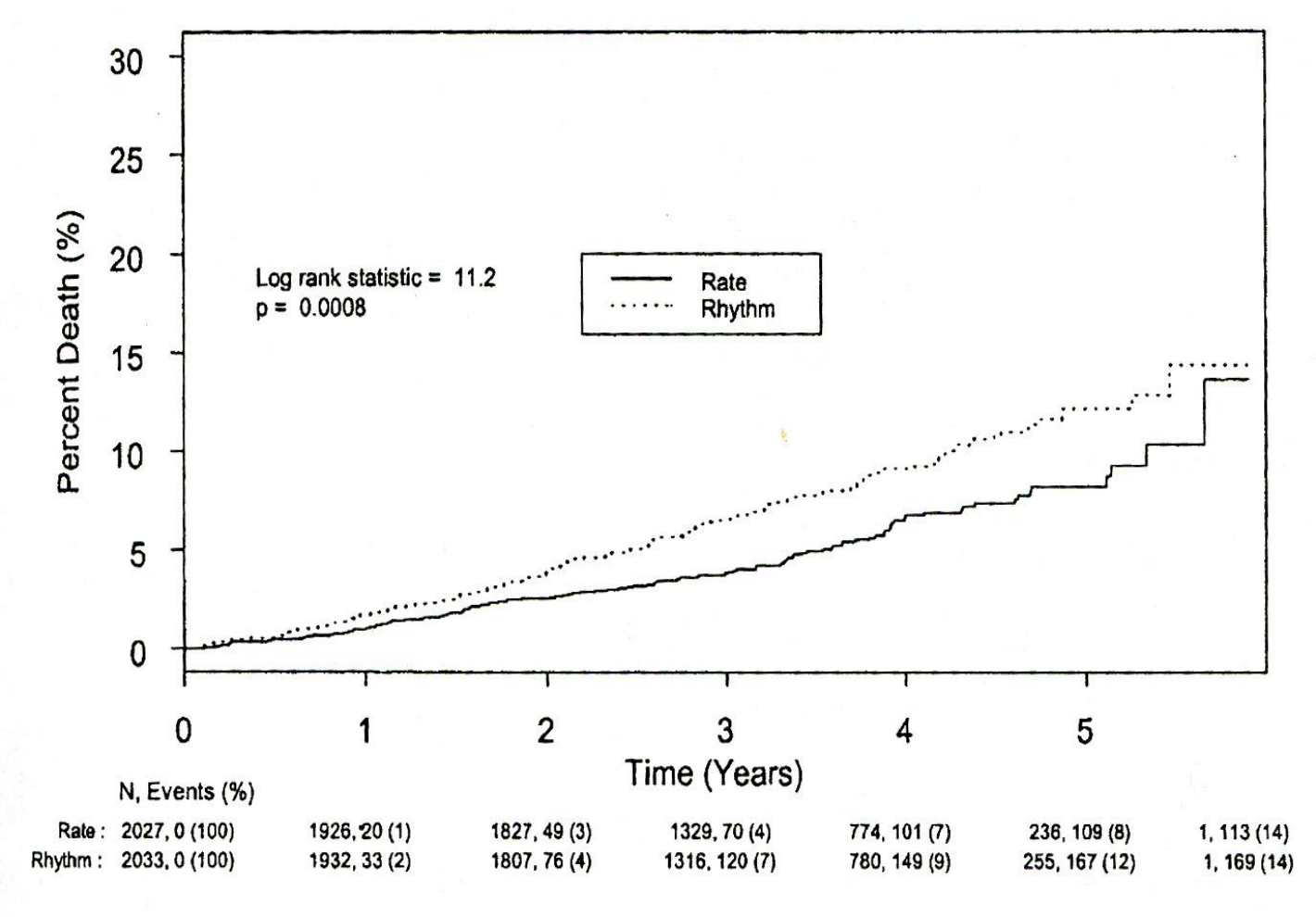
The Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) Investigators



No. of Deaths		number (percent)				
Rhythm control	0	80 (4)	175 (9)	257 (13)	314 (18)	352 (24)
Rate control	0	78 (4)	148 (7)	210 (11)	275 (16)	306 (21)

N Engl J Med 2002; 347: 1825-

Cumulative Noncardiovascular Mortality in the Rhythm-control & Rate-control Groups



Steinberg et al. Circ 2004;109:1973-80

Covariates Significantly Associated With Survival

Covariate	*P*	*HR*	*HR: 99% Confidence Limits* *Lower*	*Upper*
Age at enrollment*	0.0001	1.06	1.05	1.0
Sinus rhythm was associate with lower risk of death as was warfarin				
Congestive heart failure	0.0001	1.57	1.18	2.09
Diabetes	0.0001	1.56	1.17	2.07
Stroke or transient ischemic attack	0.0001	1.70	1.24	2.33
Smoking	0.0001	1.78	1.25	2.53
Left ventricular dysfunction	0.0065	1.36	1.02	1.81
Mitral regurgitation	0.0043	1.36	1.03	1.80
Sinus rhythm	0.0001	0.53	0.39	0.72
Warfarin use	0.0001	0.50	0.37	0.69
Digoxin use	0.0007	1.42	1.09	1.86
Rhythm-control drug use	0.0005	1.49	1.11	2.01

**Per year of age.*

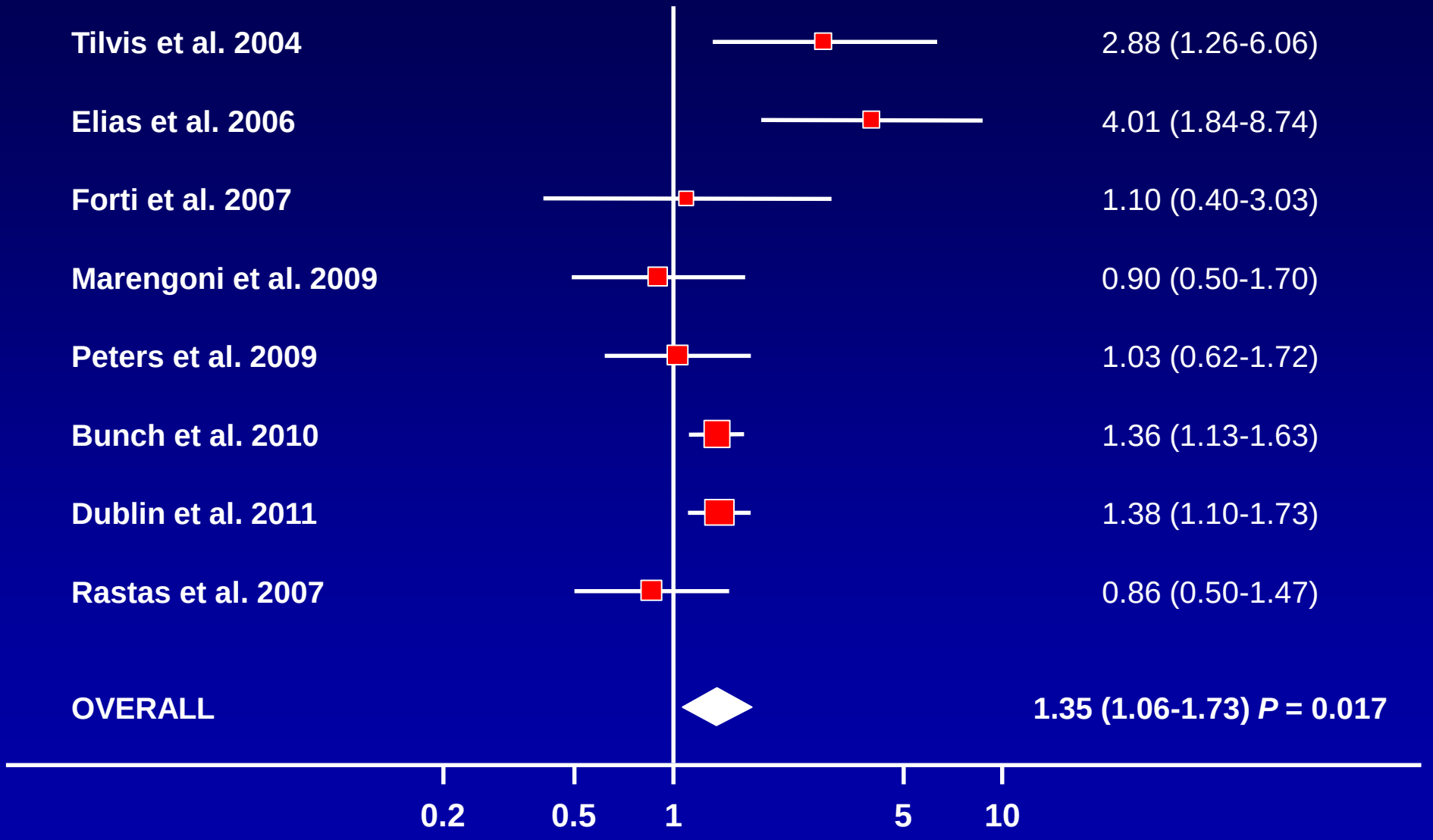
The AFFIRM Investigators. Circulation 2004; 109: 1509-13

AF and the risk of Dementia

Study	Year	Design	N. of Pts	AF Diagnosis	Dementia Diagnosis	Follow-Up (years)
Tilvis et al.	2004	Prospective observational including elderly pts in Finland	629	H&P, medical records	MMSE and CDR	5
Elias et al.	2006	Prospective observational (Framingham Offspring Study)	1011	ECG, ECG-H, H&P	Neuropsychological tests approved by a panel of neurologists and neuropsychiatrists	30
Forti et al.	2007	Prospective observational including elderly pts in Italy	431	H&P	MMSE and neuropsychological tests	4
Marengoni et al.	2009	Prospective observational including elderly pts participating to the Kungsholmen Project in Sweden	685	H&P, medical records, ICD codes	DSM-III Revised	4
Peters et al.	2009	Prospective observational including elderly pts included in the HYVET trial	3336	Not specified	DSM-IV	1.8
Bunch et al.	2010	Prospective observational including pts receiving care in the Intermountain Healthcare System in US	37025	ICD codes	ICD codes	5
Dublin et al.	2011	Prospective observational including pts receiving care in the Group Health System in US	3045	ICD codes	DSM-IV	6.8
Rastas et al.	2007	Prospective observational including elderly pts in Finland	339	ECG, ECG-H, medical records	DSM-III Revised	3.5

Santangeli, Di Biase, Natale et al., Heart Rhythm 2012

Santangeli, Di Biase, Natale et al., Heart Rhythm 2012



AF is a Substantial Cause of Morbidity and Mortality, Increasing the Risk of Stroke, Other Embolic Complications, CHF, and Death

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association®

2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society

Craig T. January, L. Samuel Wann, Joseph S. Alpert, Hugh Calkins, Joseph C. Cleveland, Jr, Joaquin E. Cigarroa, Jamie B. Conti, Patrick T. Ellinor, Michael D. Ezekowitz, Michael E. Field, Katherine T. Murray, Ralph L. Sacco, William G. Stevenson, Patrick J. Tchou, Cynthia M. Tracy and Clyde W. Yancy

Circulation. published online March 28, 2014;
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

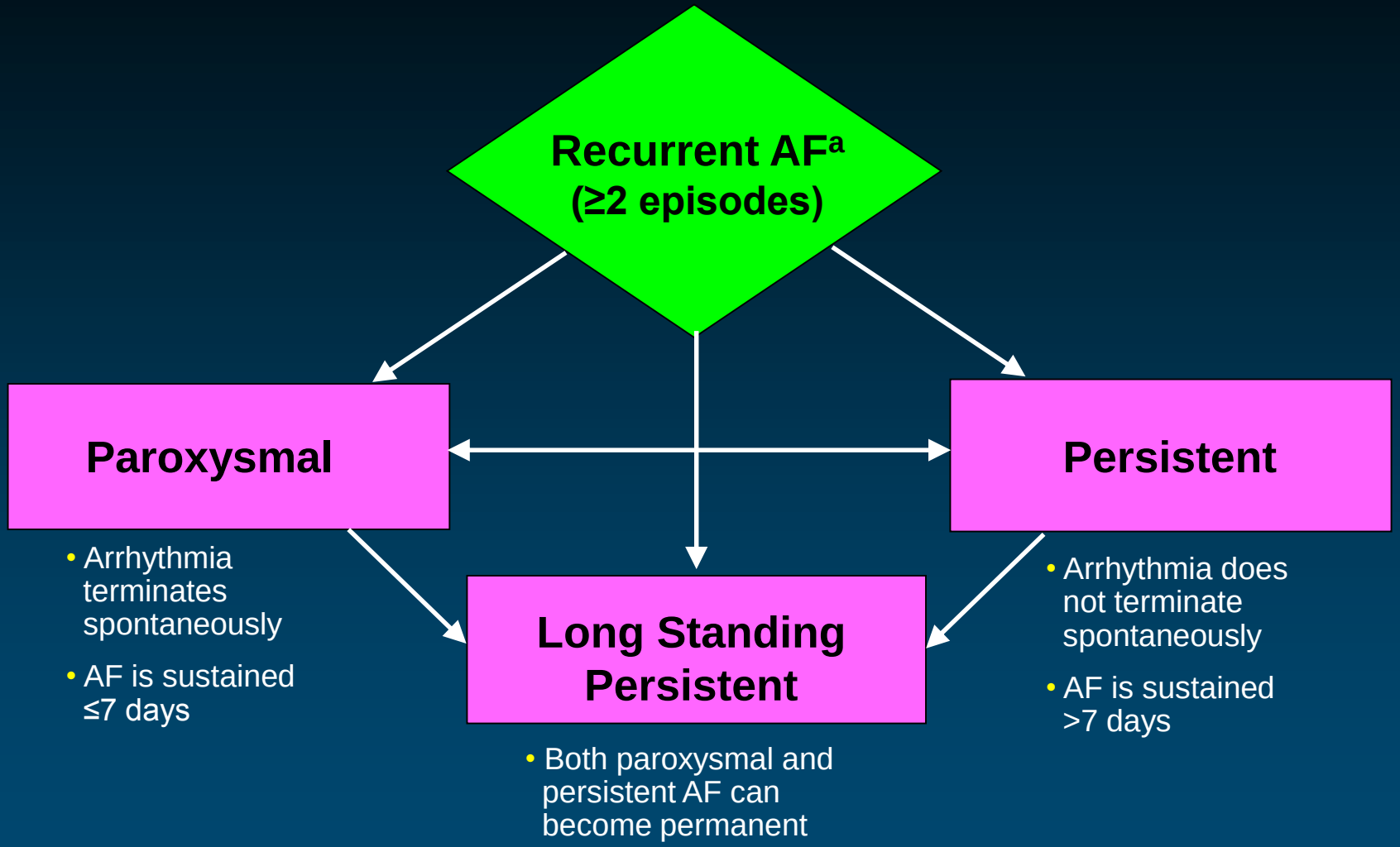
Print ISSN: 0009-7322. Online ISSN: 1524-4539

Some of the other major changes in the recommendations include:

1) **Greater use of** radiofrequency ablation for treating nonvalvular atrial fibrillation. "The efficacy of radiofrequency catheter ablation for maintaining sinus rhythm is superior to current antiarrhythmic drug therapy for maintenance of sinus rhythm in selected patient populations," the authors wrote. “ The evidence supporting the efficacy of catheter ablation is strongest for paroxysmal atrial fibrillation in younger patients with little to no structural heart disease and in procedures performed in highly experienced centers.“ They also consider long standing persistent

2) Use of a more comprehensive stroke risk calculator.
That means using the CHA2DS2-VASc score instead of the older CHADS2 score. The older score takes into account congestive heart failure, hypertension, diabetes, and prior history of stroke, transient ischemic attack, or thromboembolism, and age 75 or older. The newer score includes those variables plus vascular disease, sex, and an age range from 65 to 74. A reduced role for aspirin based on unconvincing evidence that aspirin reduces stroke risk in patients who already have a low risk.

Classification of AF

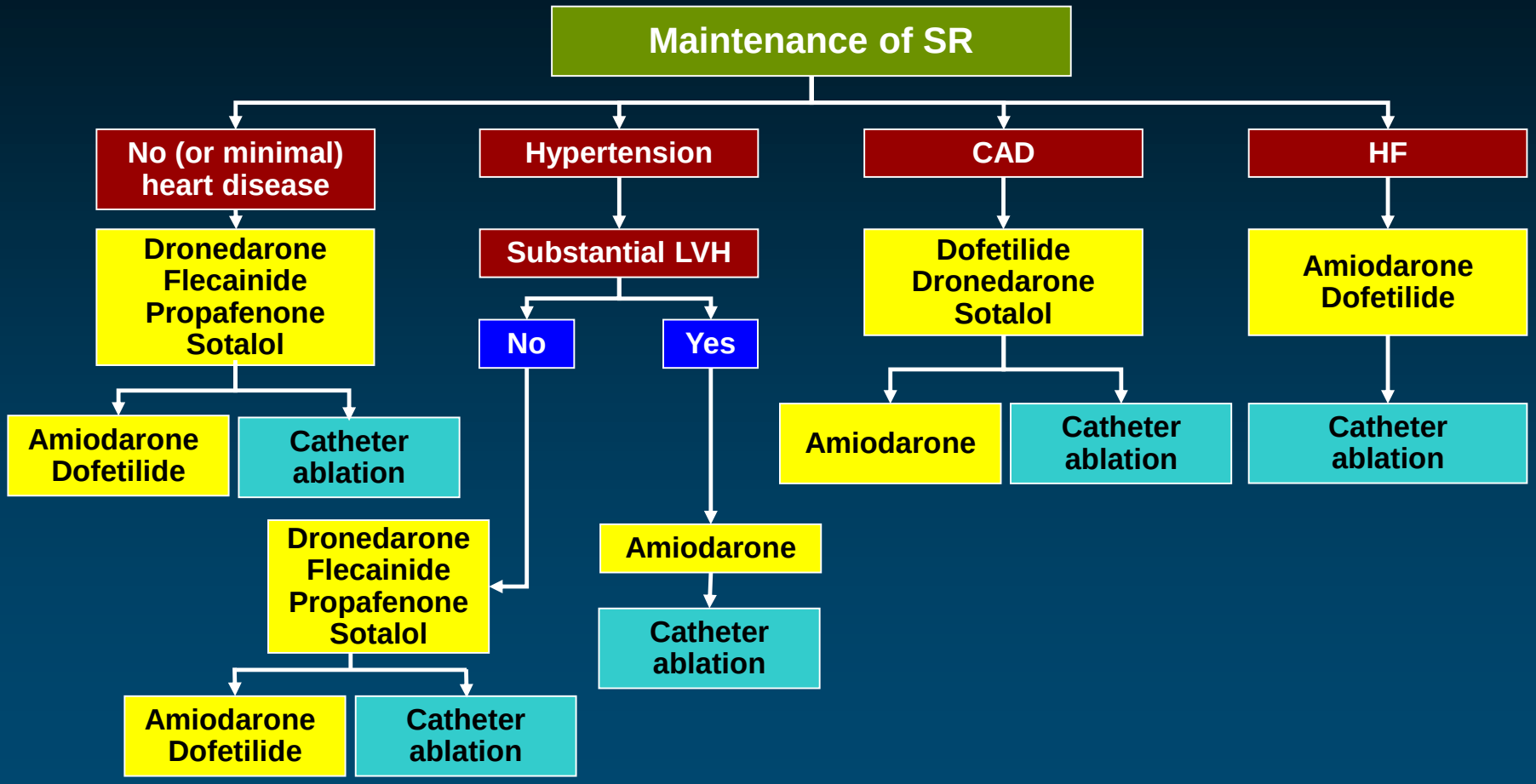


[a]Termination with pharmacologic therapy or direct-current cardioversion does not change the designation.

Fuster V, et al. *Circulation.* 2006;114(7):e257-e354.

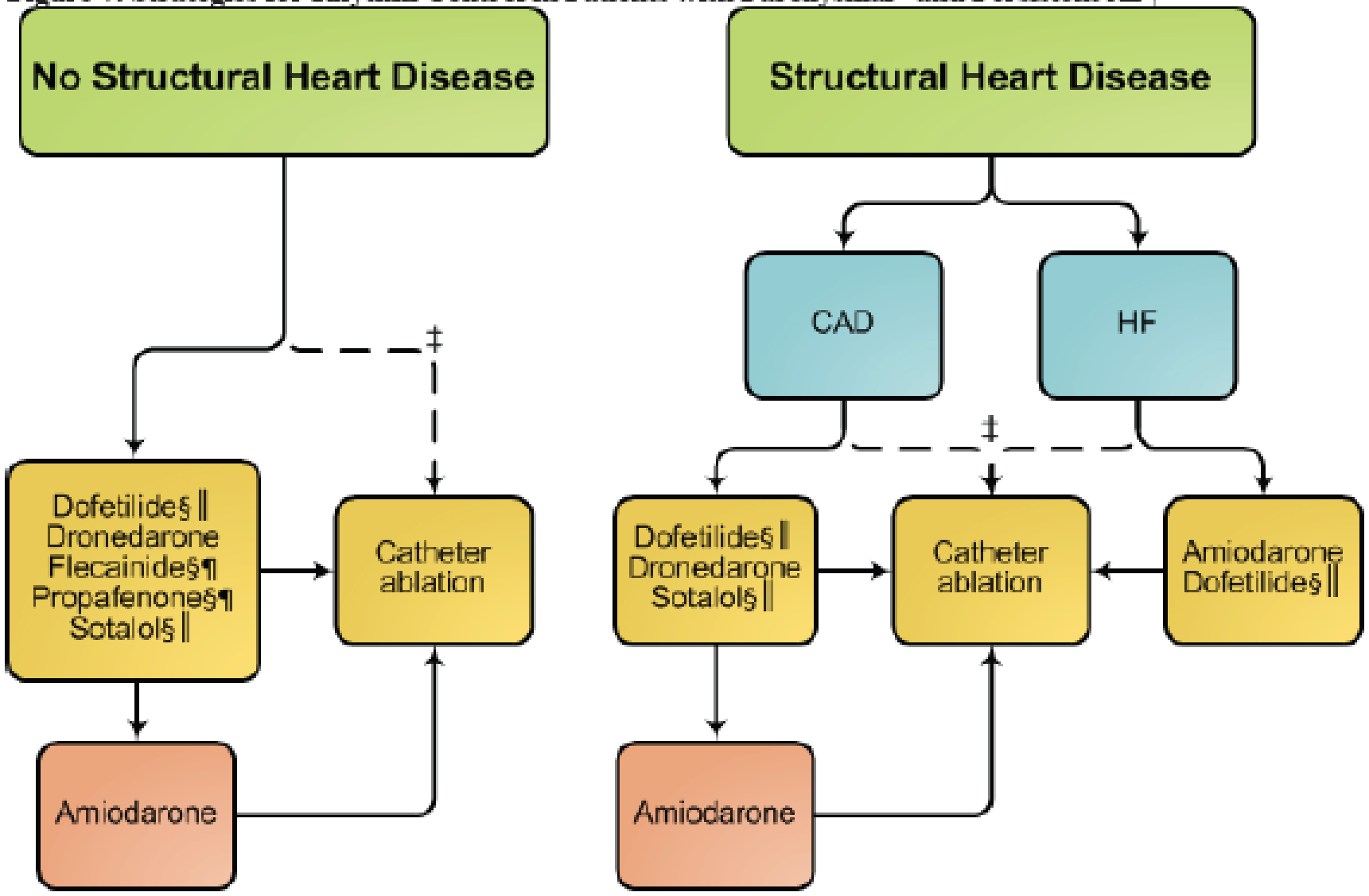
Treatment

Rhythm Control Therapies to Maintain Sinus Rhythm



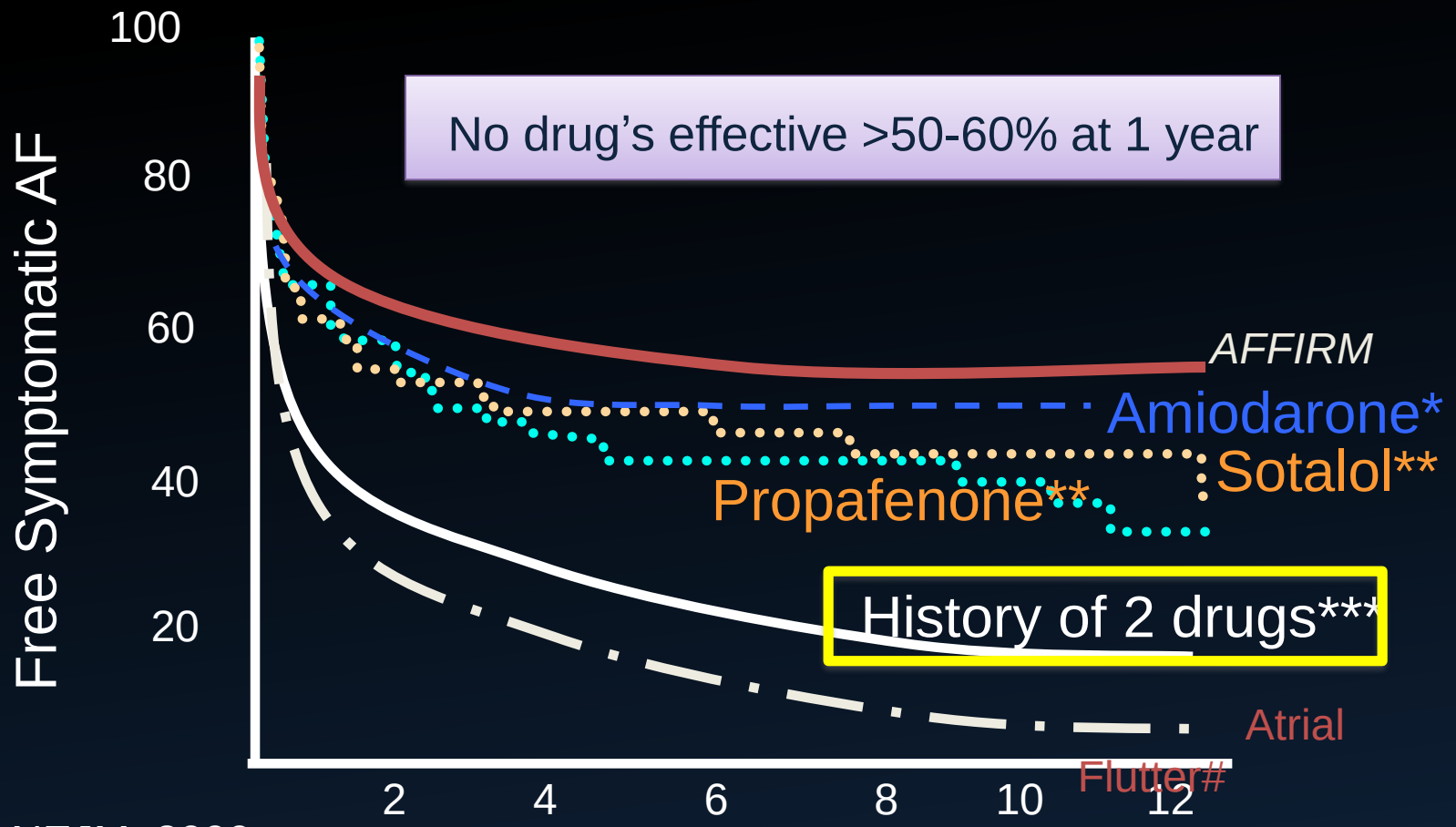
Reproduced with permission from Wann LS, et al. *Circulation*. 2011;123(1):104-123.

Figure 7. Strategies for Rhythm Control in Patients with Paroxysmal* and Persistent AF†



Atrial Fibrillation

Anti Arrhythmic Drugs



* Roy et al NEJM, 2000

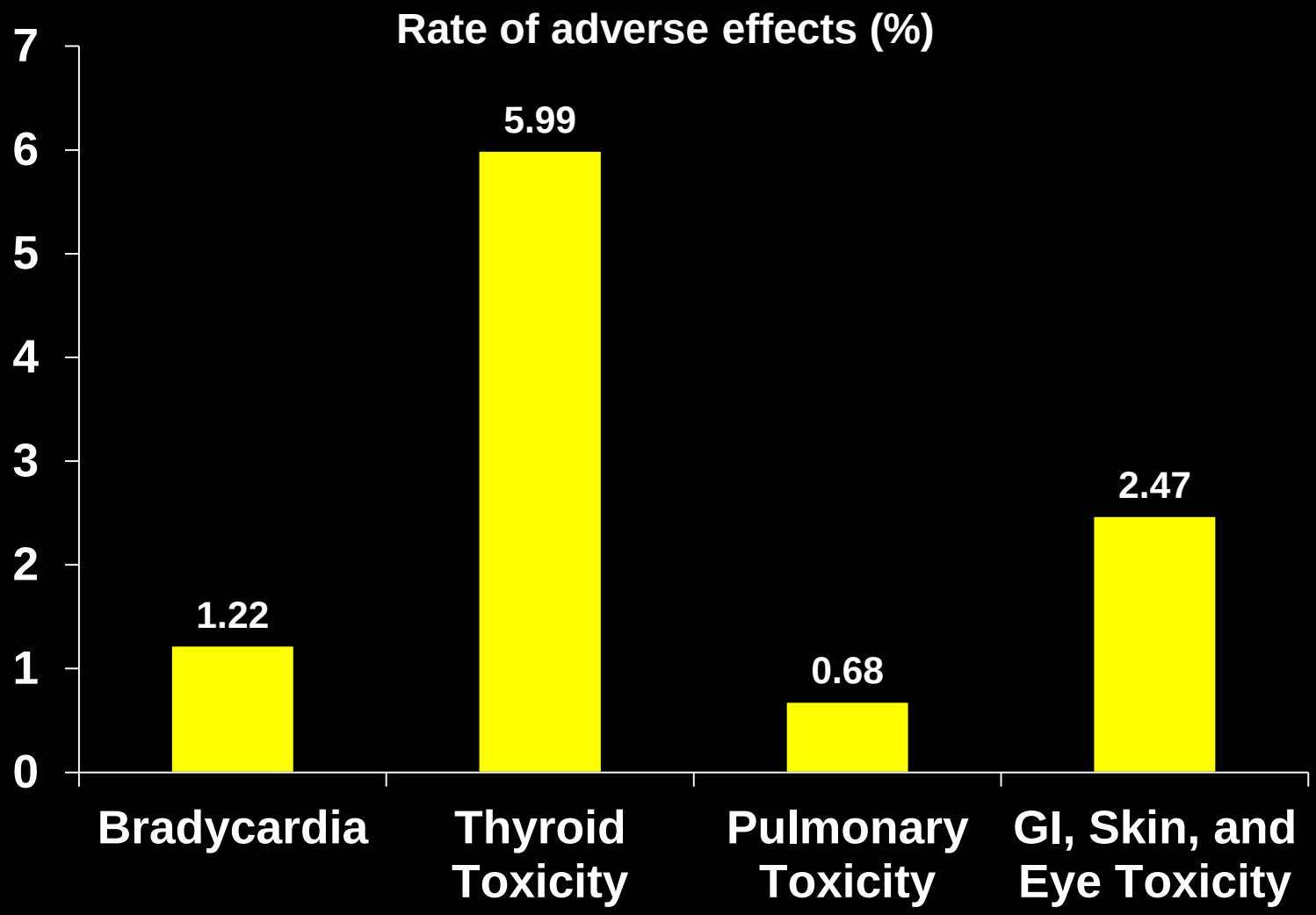
** Antman et al, JACC 1990

*** Crijns et al, AJC 1991

Natale et al JACC 2001

Adverse Effects of Amiodarone

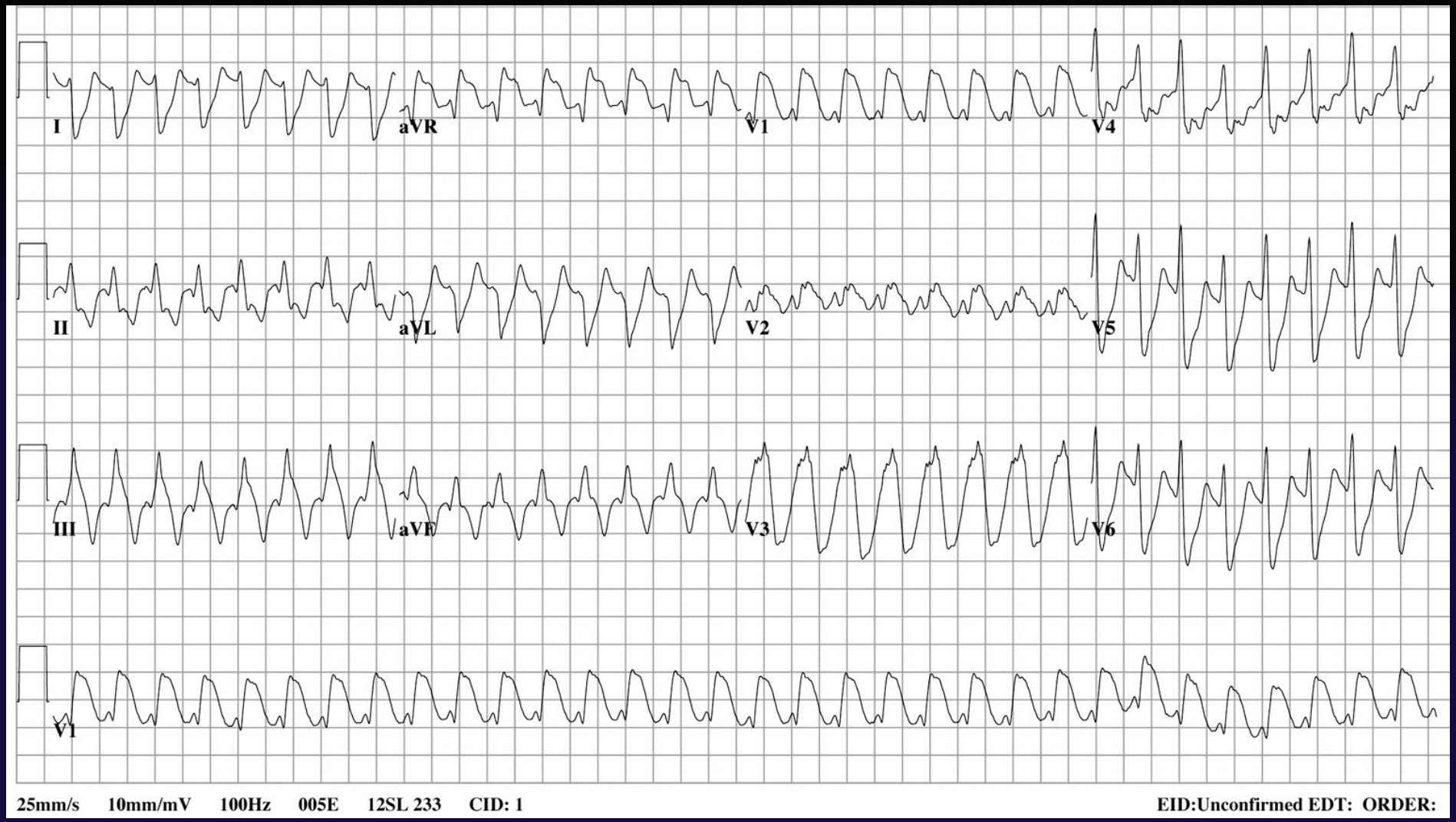
Pooled Data from 5 RCTs for the long-term SR maintenance



Amiodarone Treatment

- Do not consider young patient for treatment with amiodarone
- On amiodarone check every 6 months thyroid, liver function, and eyes for microdeposit
- Check pulmonary function once a year

A 45 yo man with history of paroxysmal atrial fibrillation was started on flecaiide and presents to ER with near syncope. On arrival a 12 lead ECG is obtained. Patient is hemodinamically stable. The most likely explanation for this clinical arrhytmia is: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V5
III
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25mm/s 10mm/mV 100Hz 005E 12SL 233 CID: 1
EID:Unconfirmed EDT: ORDER:

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1. Patient had CAD, was started on a class I AARx and now presents with ventricular tachycardia
2. An AV nodal blocker was not prescribed, so you start him on diltiazem
3. Patient was non compliant with the AARx and went back into afib

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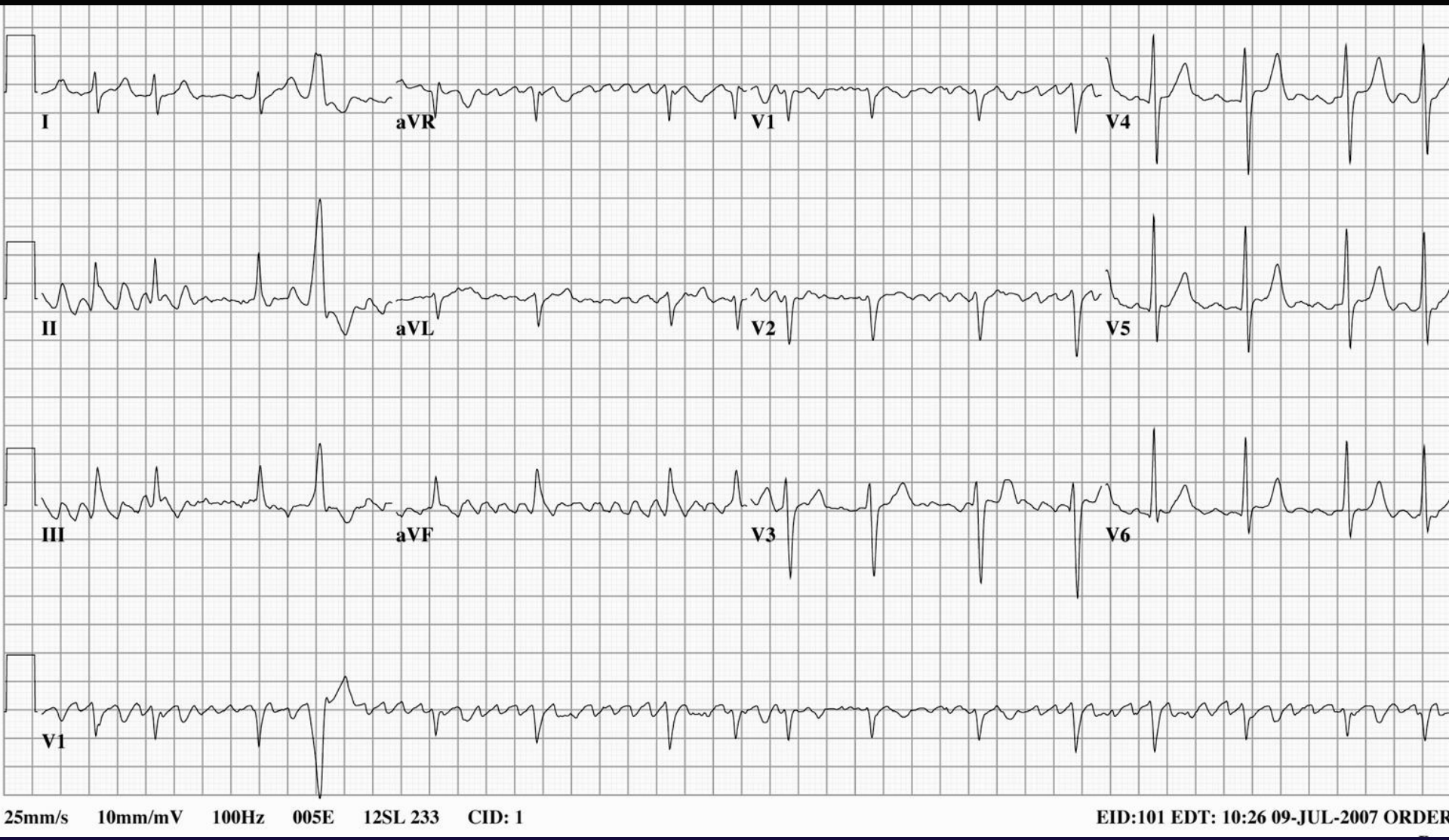
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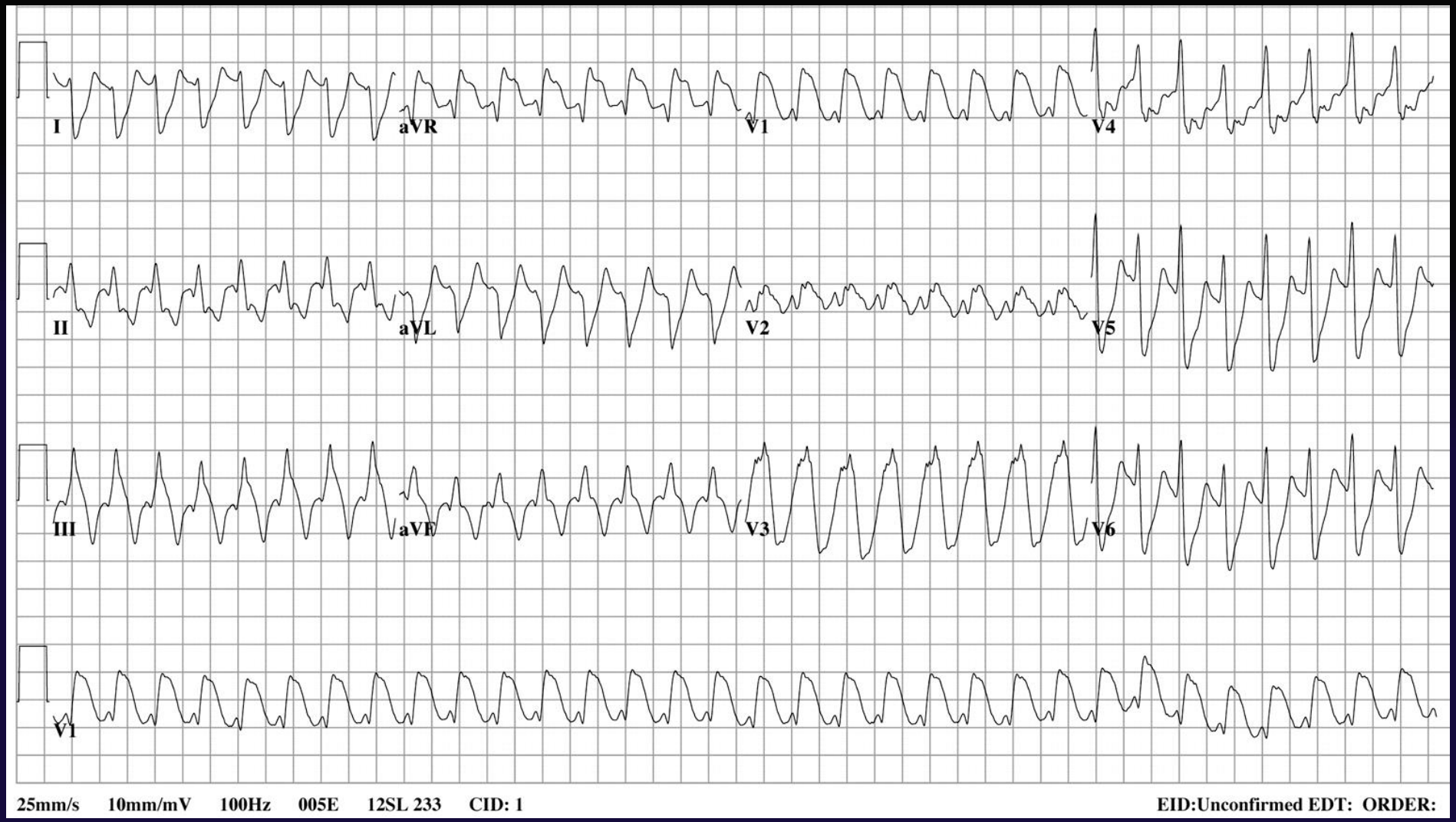
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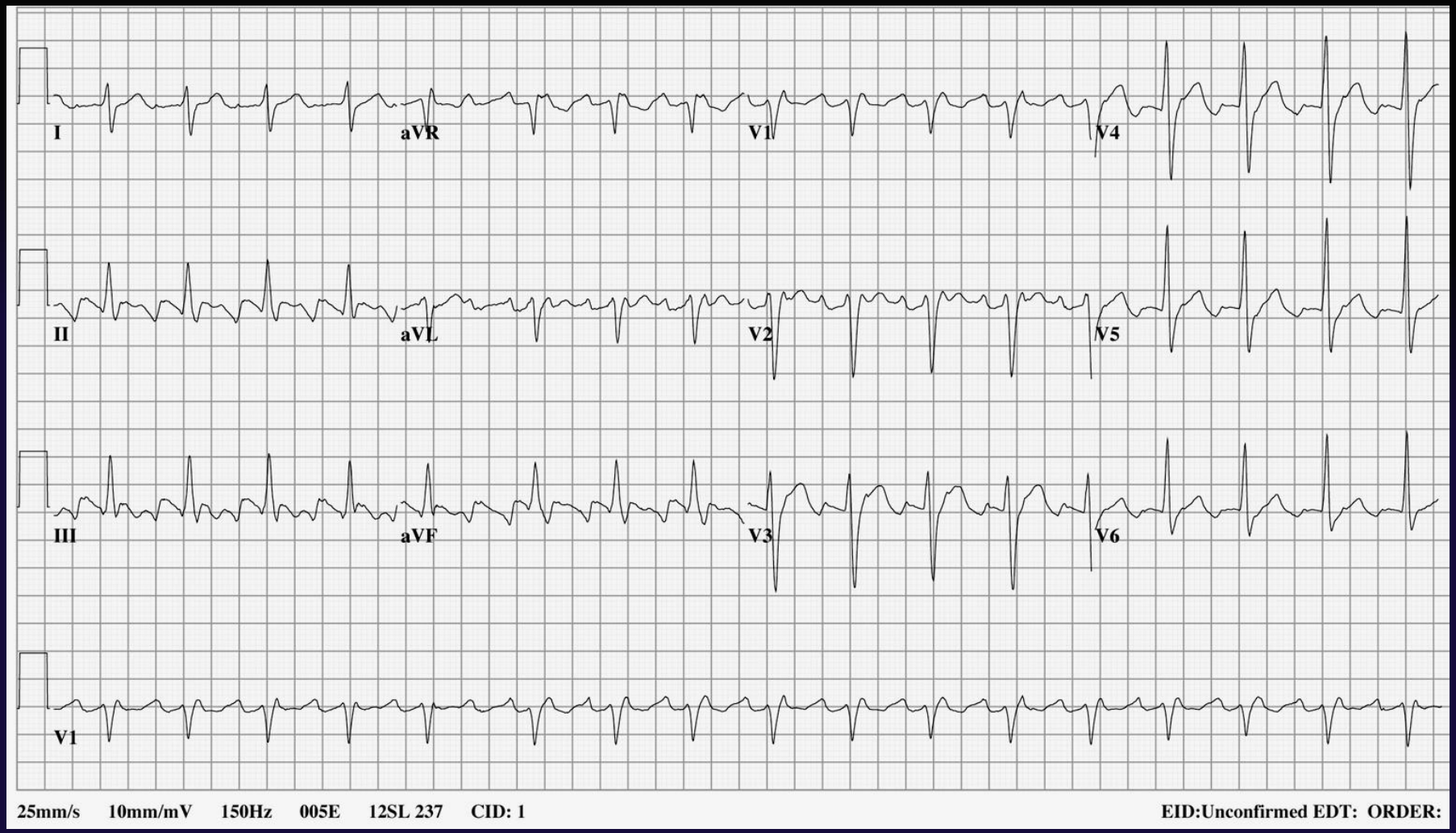
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25mm/s 10mm/mV 150Hz 005E 12SL 237 CID: 1
EID:Unconfirmed EDT: ORDER:

“Pill in the Pocket”

Candidates
- Recognized acute and recent onset with sporadic events
- No AAD risk markers
- Adequate tolerance (no pulmonary edema, syncope, etc) Test in office setting

Step 1	Step 2	Step 3
• Rate control (~100 bpm) to prevent 1:1 flutter • Short-acting CCB or β-blocker	• Propafenone 600 mg (single dose) • Flecainide 300 mg (single dose)	• Observe for effect and tolerance (first episode)

Subsequent events
- Treat at home (convenient and inexpensive)
- Improves QoL, reduces ER visits/hospitalization, costs

Acute load on chronic therapy
- 2 extra “pill in the pocket” dosing regimens have been used to treat breakthrough episodes (max. daily dose vs substitute bolus dose)[a]

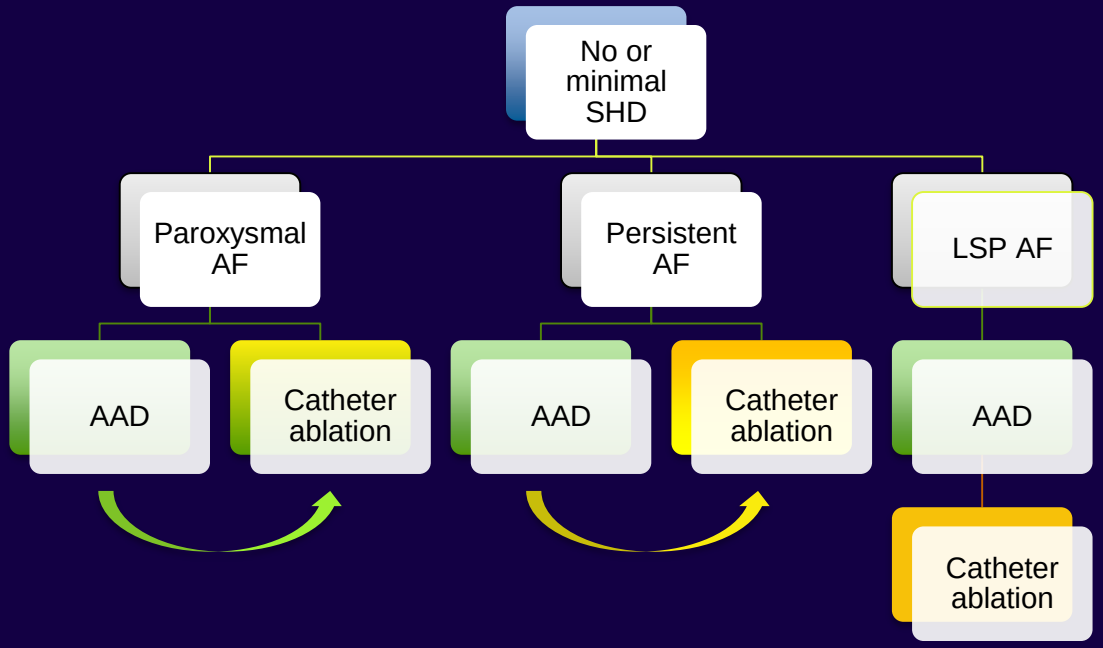
Alboni P, et al. *N Engl J Med.* 2004;351(23):2384-2391.

[a]Reiffel JA. *Pacing Clin Electrophysiol*. 2009;32(8):1073-1084.

Catheter Ablation

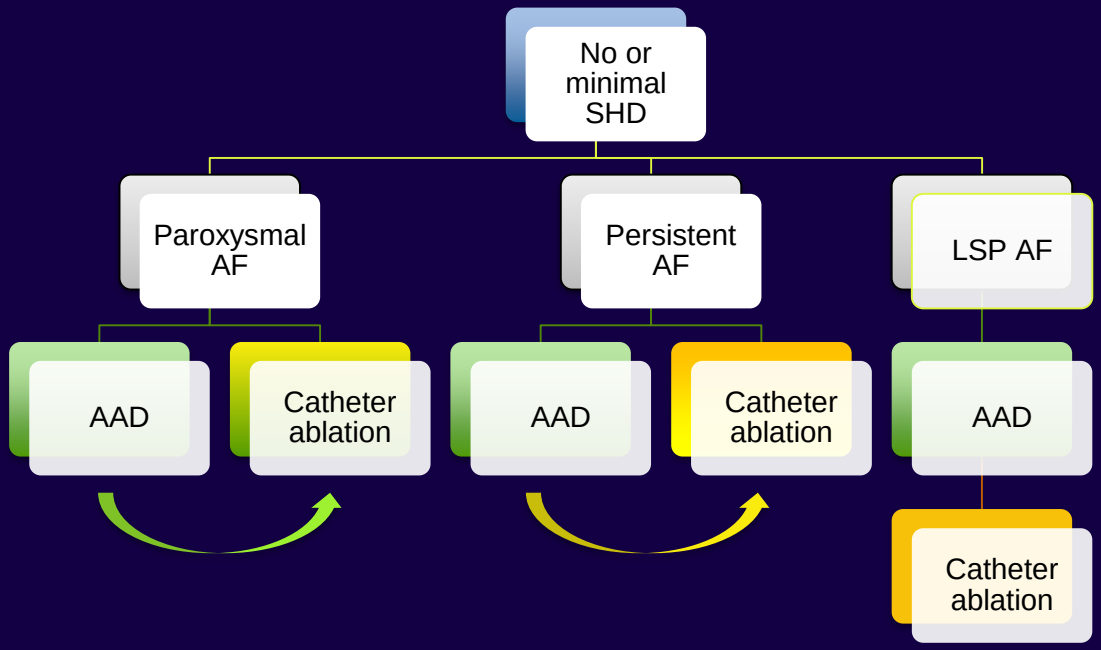
AF Catheter Ablation: Initial Considerations

- Candidates for ablation



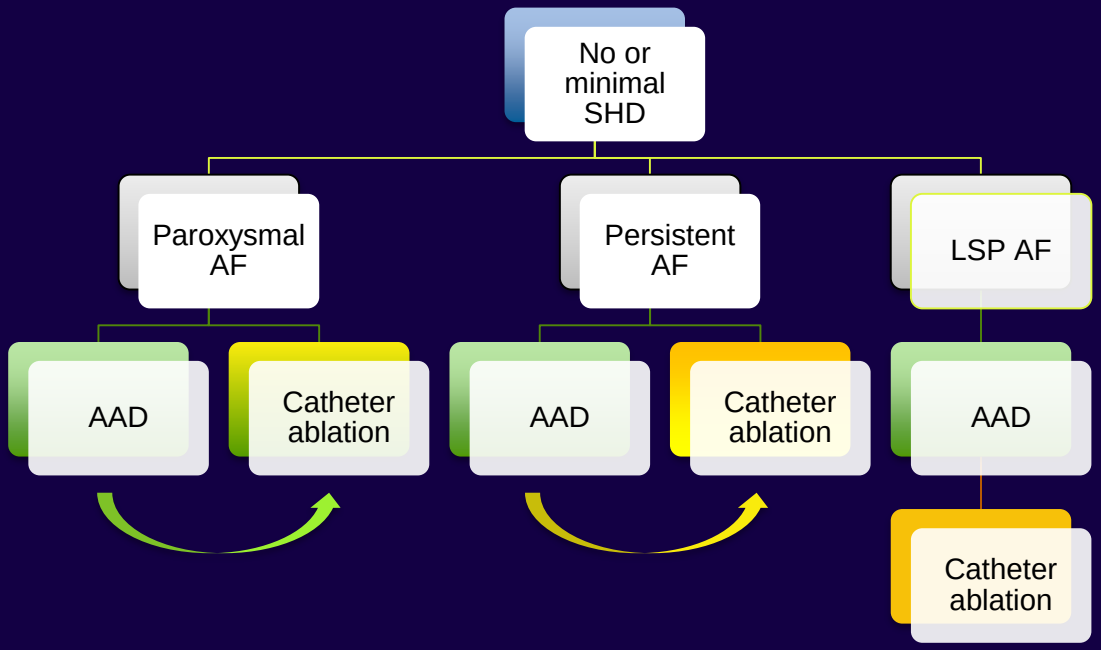
- Symptomatic PAF refractory to ≥ 1 AAD
  Class I LoE A
- Symptomatic PAF first line therapy
  Class IIa LoE B

January C et al
2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation



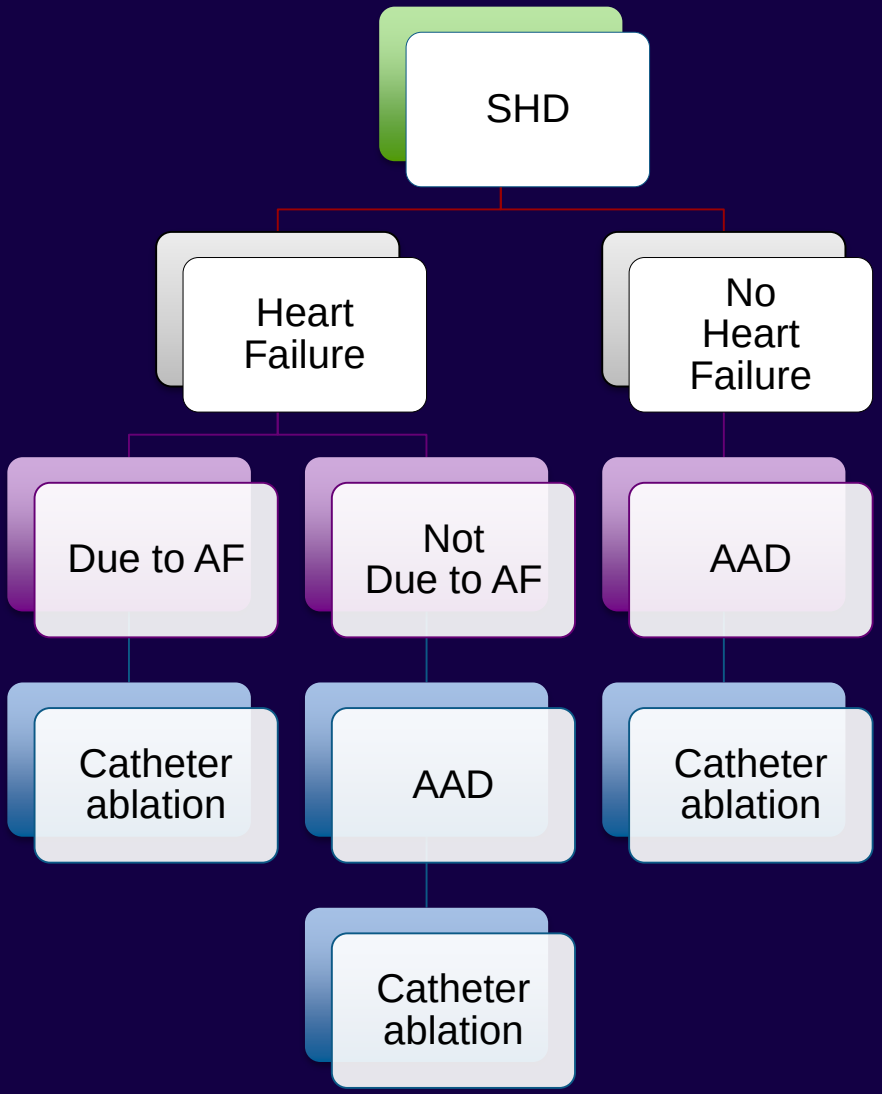
- Symptomatic PerAF refractory to ≥ 1 AAD
  Class IIa LoE A
- Symptomatic PerAF first line therapy
  Class IIb LoE C

January C et al
2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation
J Am Coll Cadiol 2014;64(21):e1–e76



- Symptomatic LSPAF refractory to ≥ 1 AAD
  Class IIb LoE B

January C et al
2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation
J Am Coll Cadiol 2014;64(21):e1–e76



January C et al
2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation

Ablation vs. Amiodarone for Treatment of Atrial Fibrillation in Patients with Congestive Heart Failure and an Implanted ICD/CRT-D

AATAC-AF

Persistent AF with symptomatic HF, LVEF ≤ 40%, CIED

N = 203

PVAI ± triggers

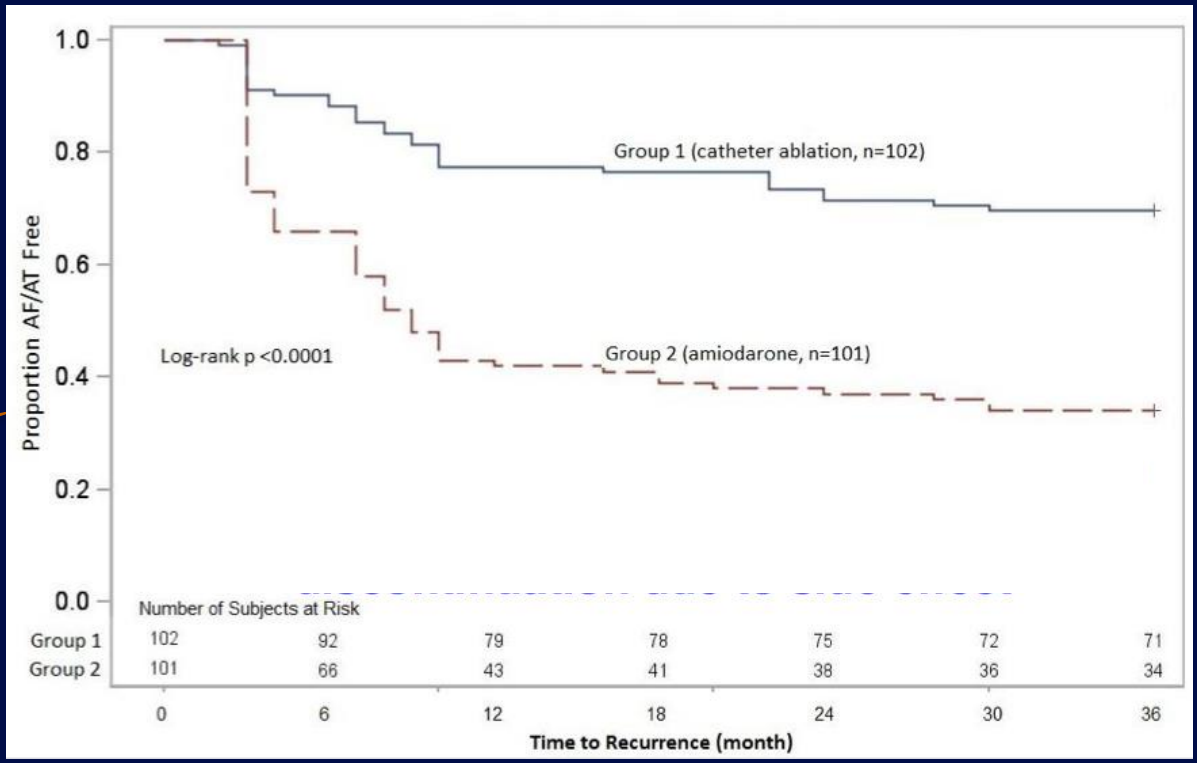
Amiodarone

Freedom from AT/AF

FU = 24 months

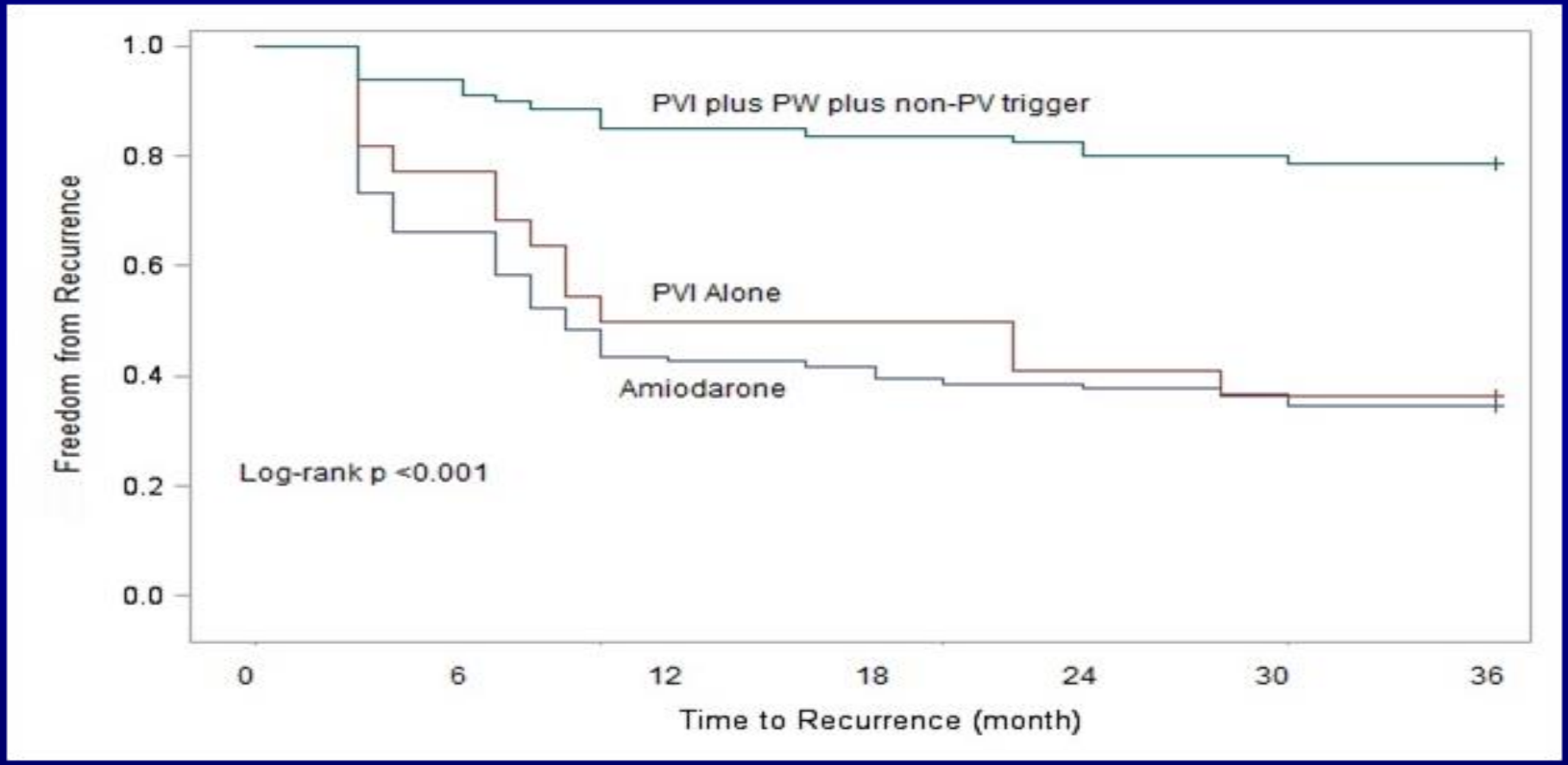
Mortality benefit

70 vs 34 %
(p < 0.0001)



Di Biase L, Natale A et al Circulation 2016

Pulmonary Vein Isolation Alone Is Not Superior To Amiodarone for the Treatment Of Persistent Atrial Fibrillation In Patients With Congestive Heart Failure and an Implanted Device: Results From The AATAC Randomized Trial



Di Biase, Natale, et al Circulation 2016

Catheter Ablation versus Standard conventional Treatment in patients with LEft ventricular dysfunction and Atrial Fibrillation

The CASTLE-AF trial

Nassir F. Marrouche and Johannes Brachmann,
on behalf the CASTLE AF Investigators

Primary Endpoint

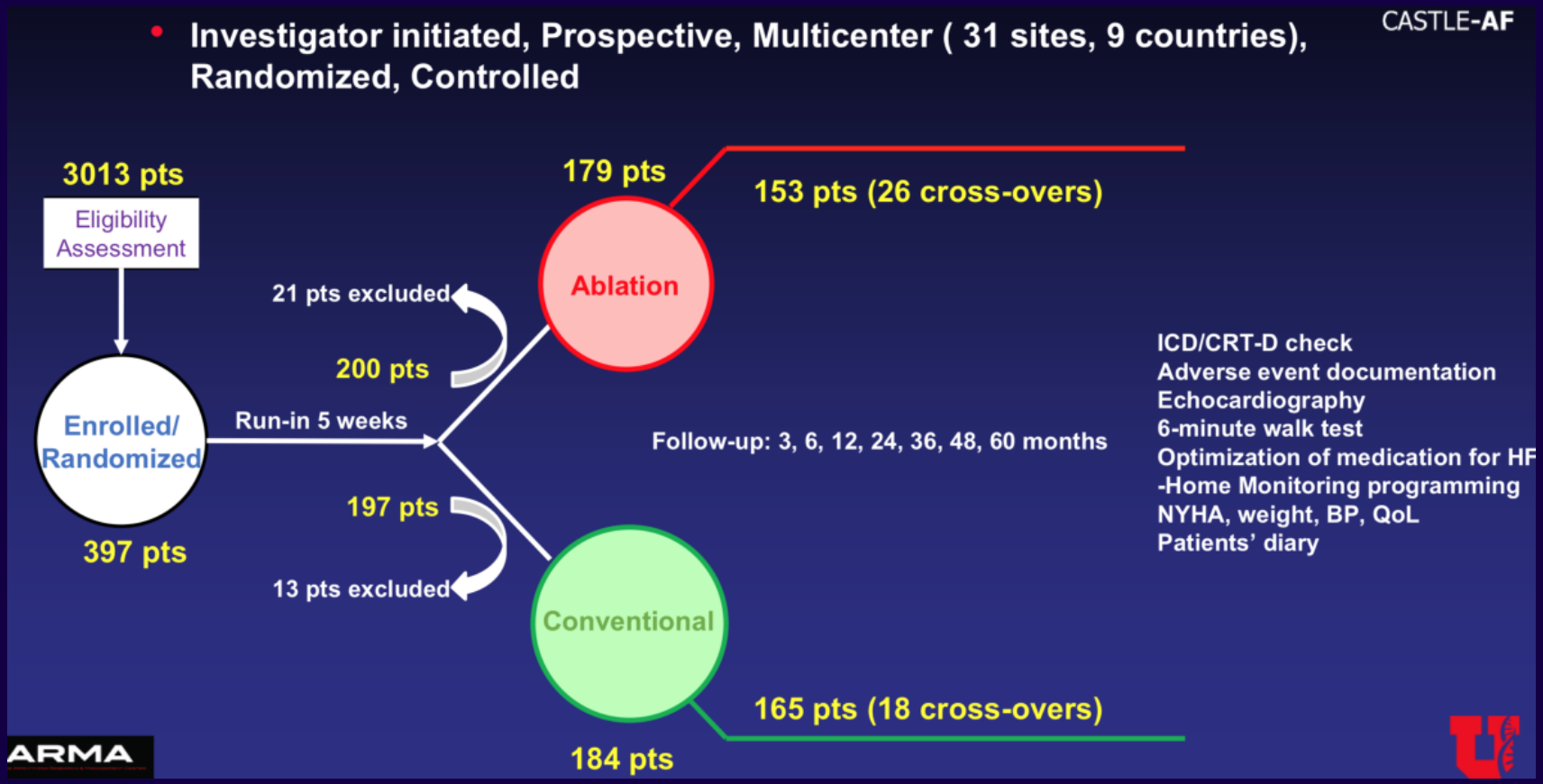
- ***All-cause mortality***
- ***Worsening heart failure admissions***

Secondary Endpoints

- All-cause mortality
- Hospitalization due to worsening of heart failure
- Cerebrovascular accidents
- Cardiovascular mortality
- Unplanned hospitalization due to cardiovascular reason
- All-cause hospitalization
- Quality of Life: Minnesota Living with Heart Failure and EuroQoL EQ-5D
- Exercise tolerance (6 minutes walk test)
- Number of delivered ICD shocks, and ATPs (appropriate/inappropriate)
- LVEF
- Time to first ICD shock, and time to first ATP
- Number of device detected VT/VF
- AF burden: cumulative duration of AF episodes
- AF free interval: time to first AF recurrence after 3 months blanking period post ablation

- Symptomatic paroxysmal or persistent AF
- Failure or intolerance to ≥ 1 or unwillingness to take AAD
- LVEF ≤ 35%
- NYHA class ≥ II
- ICD/CRTD with Home Monitoring™ capabilities already implanted due to primary or secondary prevention

Primary composite endpoint
- all-cause mortality
- unplanned hospitalization for worsening HF



Conventional RX per 2006 ACC/AHA/ESC guidelines

- rhythm control if possible
- rate control with HR 60-80 at rest and 90-115 during moderate exercise
- OAC

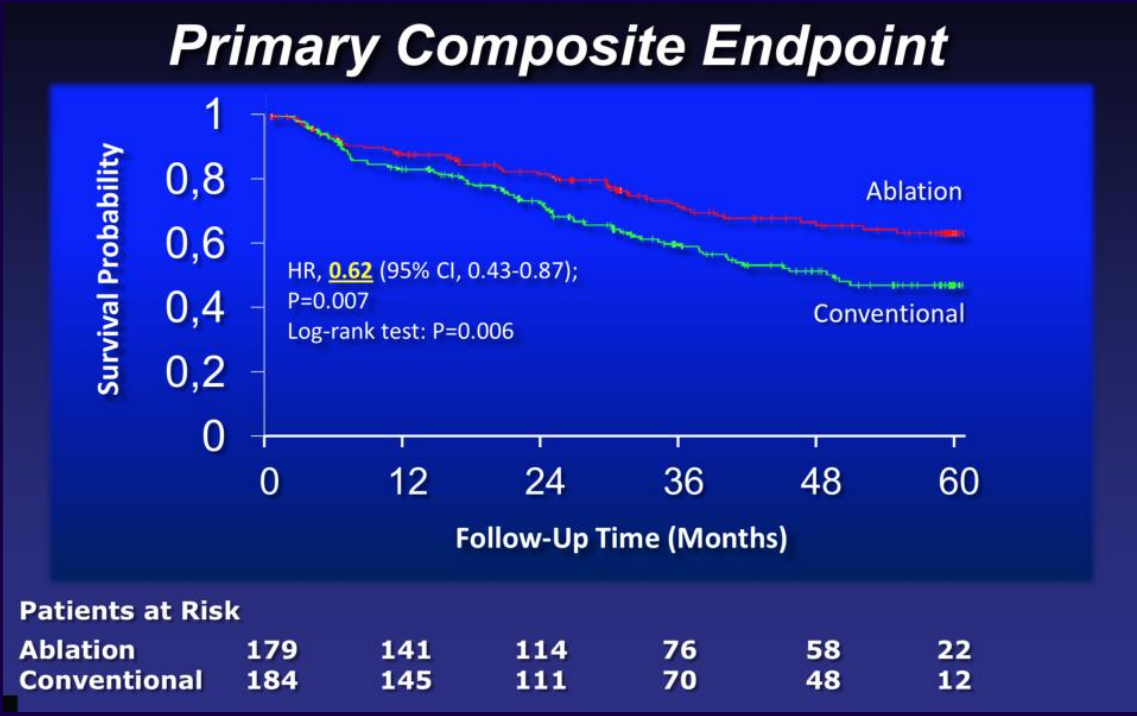
RF

- PVI
- additional lesions per operator choice
- repeat procedure after BP

	Ablation group (179 patients)	Conventional group (184 patients)
†Age – years	64 (56-71)	64 (56-73.5)
New York Heart Association class		
I (%)	11	11
II (%)	58	61
III (%)	29	27
IV (%)	2	1
†Left ventricular ejection fraction – %	32.5 (25.0-38.0)	31.5 (27.0-37.0)
Current type of atrial fibrillation		
Paroxysmal (%)	30	35
Persistent (%)	41	35
Long-standing persistent (>1-year) (%)	28	30
§CRT-D implanted (%)	27	28
§ICD implanted (%)	73	72

ACE-inhibitor or ARB – no. (%)	94	91
Beta-blocker – no. (%)	93	95
Diuretic – no. (%)	93	93
Digitalis – no. (%)	18	31
Oral anticoagulant – no. (%)	93	96
Antiarrhythmic drug – no. (%)	32	30
Amiodarone – no. (%)	97	85

Over a median FU of 37.8 months:
- composite primary endpoint
28.5% (RF) vs 44.6% (Rx)
HR 0.62 (0.43-0.87; P=0.006)
- all-cause mortality
13.4% (RF) vs 25% (Rx)
HR 0.53 (0.32-0.86; P=0.009)
- HF hospitalizations
20.7% vs 35.9%
HR 0.49 (0.29-0-84; P = 0.008)



Patient History

- 67 year old female with highly symptomatic paroxysmal atrial fibrillation who was given amiodarone subsequently discontinued for side effect
- Echo normal, left atrium 3.7
- Mild hypertension no other medical issues

What would you do next?

- 1) Give flecainide
- 2) Consider rate control
- 3) AV node ablation
- 4) Pulmonary vein ablation

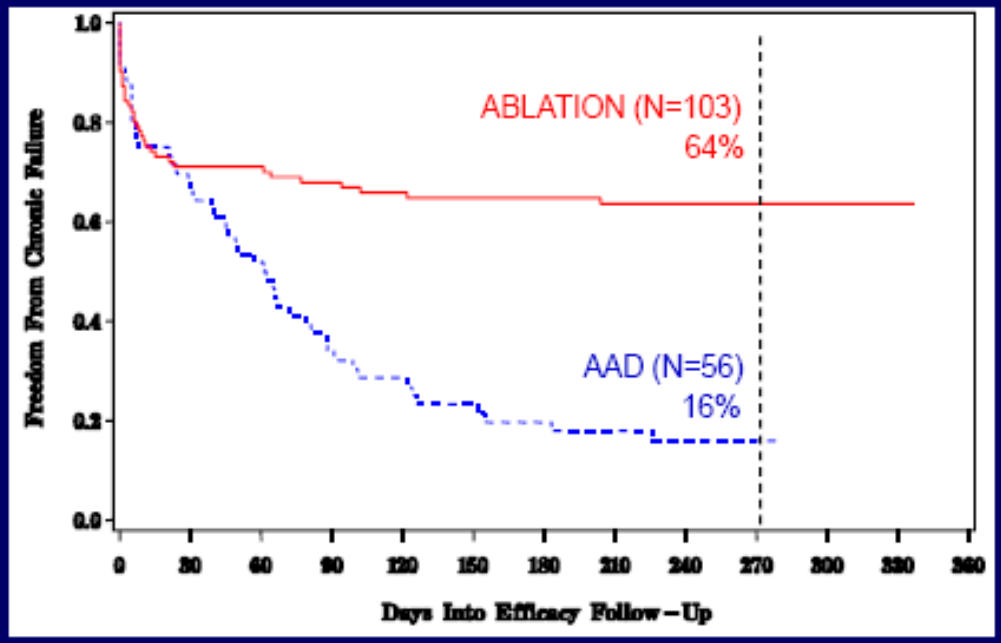
Recently Completed Study
Ablation *vs* AADs: 1 yr Success

Study	AADs Success Rate	Ablation Success Rate	2nd Ablations	Still on AADs
A4	23%	89%	80%	0%
Thermocool IDE	17%	63%	13%	7%
STOP-AF	7%	70%	19%	12%
CABANA Pilot	38%	61%	21%	28%

Comparison of Antiarrhythmic Drug Therapy and Radiofrequency Catheter Ablation in Patients with Paroxysmal Atrial Fibrillation: The ThermoCool AF Trial

David J Wilber, Loyola Univ Medical Ctr, Maywood, IL; Carlo Pappone, Hosp San Raffaele, Milan, Italy; Petr Neuzil, Na Homolce Hosp, Prague, Czech Republic; Angelo De Paola, Hosp Sao Paulo, Sao Paulo, Brazil; Frank E Marchlinski, Univ of Pennsylvania, Philadelphia, PA; Andrea Natale, Cleveland Clinic Fndn, Cleveland, OH; Laurent Macle, Montreal Heart Inst, Montreal, QC, Canada; Hugh Calkins, Johns Hopkins Hosp, Baltimore, MD; Emile Daoud, Ohio State Univ, Columbus, OH; Burr Hall, Univ of Rochester Medical Center, Rochester, NY

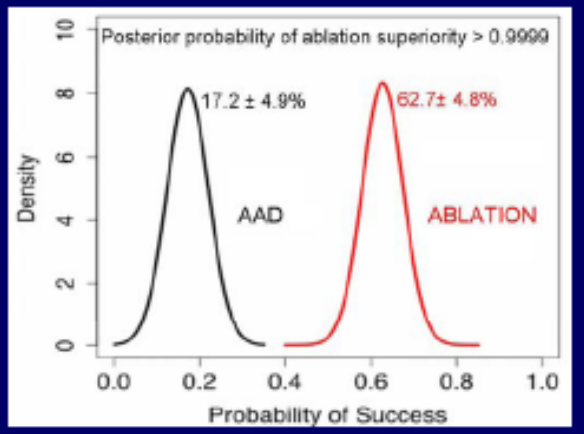
Primary Endpoint Analysis



KM curve of time to protocol adjudicated chronic failures by randomization group (n=159), $p < 0.001$, log rank test

12/36 ablation, and 7/47 AAD protocol adjudicated chronic failures not due to recurrent symptomatic AF

Bayesian posterior probabilities of outcome



Catheter Ablation Versus Antiarrhythmic Drugs for Atrial Fibrillation

The A4 Study

Pierre Jaïs, MD; Bruno Cauchemez, MD; Laurent Macle, MD; Emile Daoud, MD; Paul Khairy, MD, PhD; Rajesh Subbiah, BSc (Med), MBBS, PhD; Mélèze Hocini, MD; Fabrice Extramiana, MD; Fréderic Sacher, MD; Pierre Bordachar, MD; George Klein, MD; Rukshen Weerasooriya, MBBS; Jacques Clémenty, MD; Michel Haïssaguerre, MD

Background—The mainstay of treatment for atrial fibrillation (AF) remains pharmacological; however, catheter ablation has increasingly been used over the last decade. The relative merits of each strategy have not been extensively studied.

Methods and Results—We conducted a randomized multicenter comparison of these 2 treatment strategies in patients with paroxysmal AF resistant to at least 1 antiarrhythmic drug. The primary end point was absence of recurrent AF between months 3 and 12, absence of recurrent AF after up to 3 ablation procedures, or changes in antiarrhythmic drugs during the first 3 months. Ablation consisted of pulmonary vein isolation in all cases, whereas additional extrapulmonary vein lesions were at the discretion of the physician. Crossover was permitted at 3 months in case of failure. Echocardiographic data, symptom score, exercise capacity, quality of life, and AF burden were evaluated at 3, 6, and 12 months by the supervising committee. Of 149 eligible patients, 112 (18 women [16%]; age, 51.1±11.1 years) were enrolled and randomized to ablation (n=53) or "new" antiarrhythmic drugs alone or in combination (n=59). Crossover from the antiarrhythmic drugs and ablation groups occurred in 37 (63%) and 5 patients (9%), respectively (P=0.0001). At the 1-year follow-up, 13 of 55 patients (23%) and 46 of 52 patients (89%) had no recurrence of AF in the antiarrhythmic drug and ablation groups, respectively (P<0.0001). Symptom score, exercise capacity, and quality of life were significantly higher in the ablation group.

Conclusion—This randomized multicenter study demonstrates the superiority of catheter ablation over antiarrhythmic drugs in patients with AF with regard to maintenance of sinus rhythm and improvement in symptoms, exercise capacity, and quality of life. (***Circulation***. **2008;118:2498-2505.**)

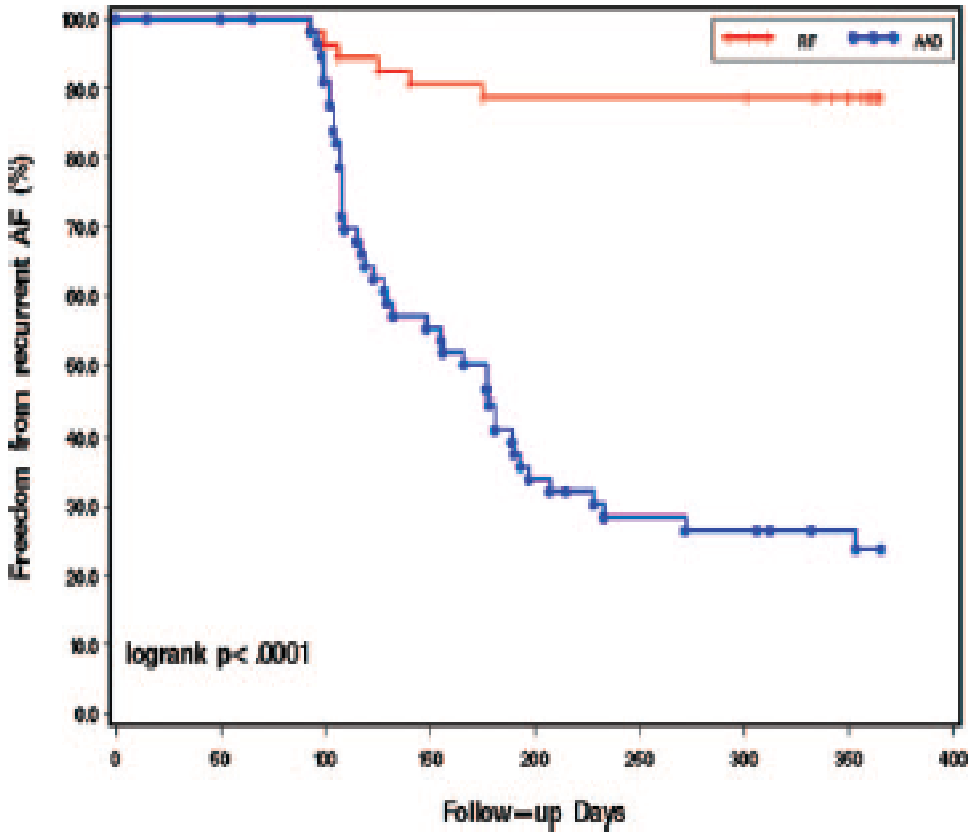
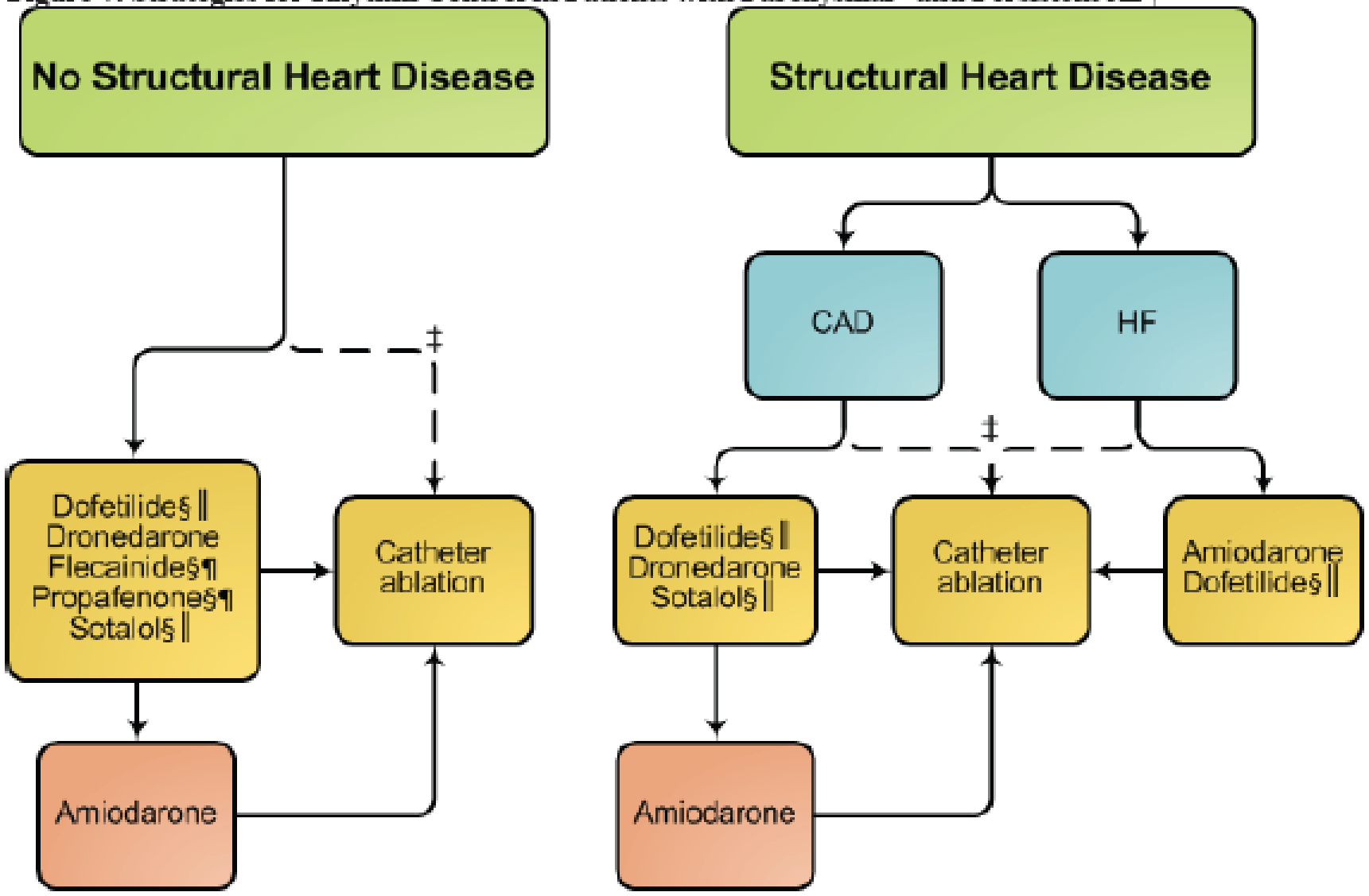


Figure 1. Kaplan–Meier analysis for time to recurrent AF after the 90-day treatment adjustment period for both groups.

Figure 7. Strategies for Rhythm Control in Patients with Paroxysmal* and Persistent AF†



First Line Ablation

RAAFT-2

First Line *R*adiofrequency *A*blation versus *A*ntiarrhythmic Drugs for Atrial *F*ibrillation *T*reatment: A Multicentre Randomized Trial

CO-PI

Andrea Natale – Carlos A. Morillo

Carlos A. Morillo, Atul Verma, Karl H. Kuck, Girish M. Nair, Jean Champagne, Lawrence Sterns, Heather Beresh, Purnima Rao-Melancini, Stuart J. Connolly and Andrea Natale, on behalf of the RAAFT-2 investigators.

Sponsor: Population Health Research Institute
McMaster University and Hamilton Health Sciences

Grant-in-Aid: Biosense Webster Inc., a Johnson & Johnson Co.

McMaster University HEALTH SCIENCES

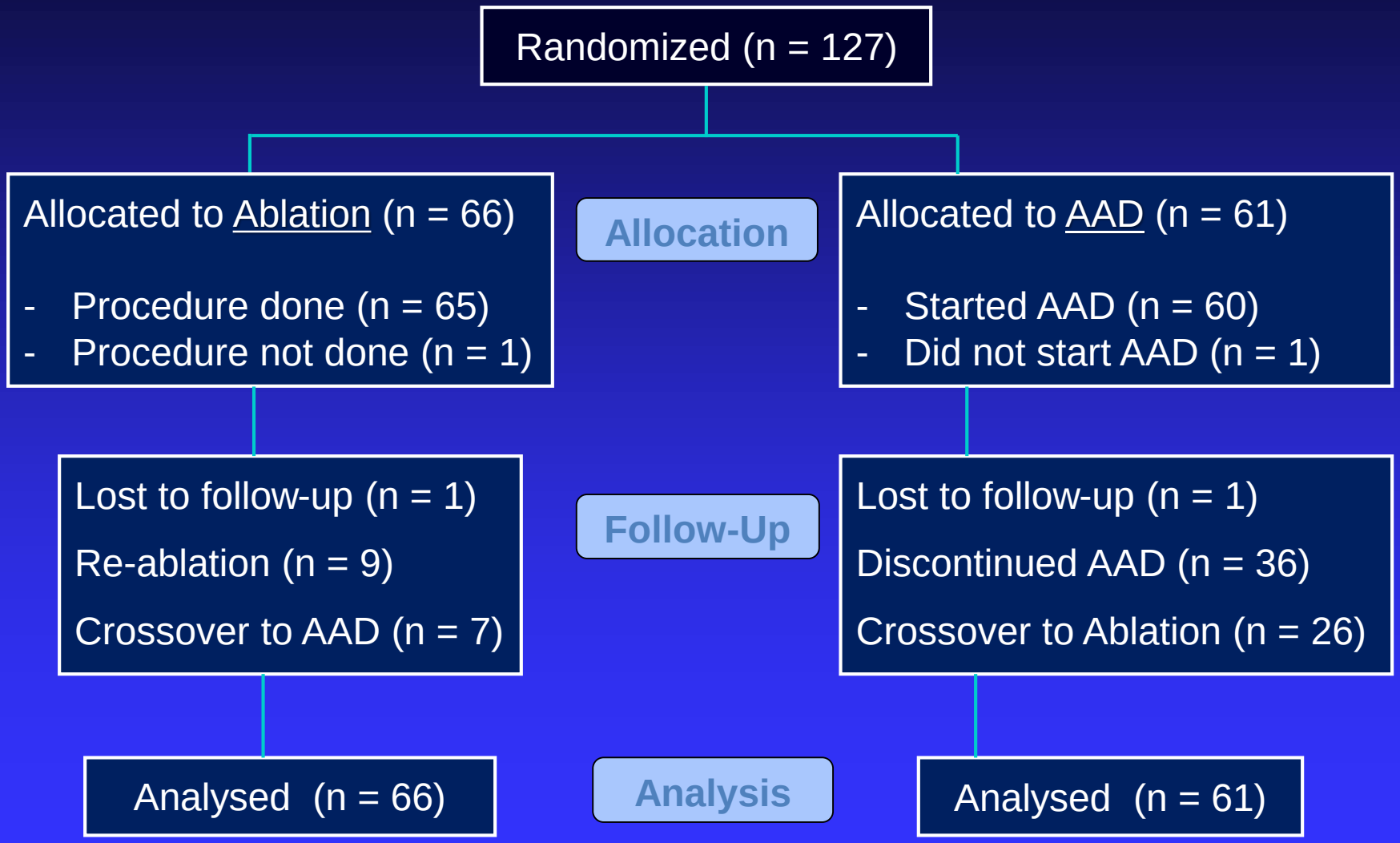
JAMA 2014

Population Health Research Institute
Hamilton Health Sciences/McMaster University

Primary Study Objective

To assess whether catheter-based pulmonary vein isolation is superior to antiarrhythmic drugs as **first line therapy** in patients with symptomatic paroxysmal recurrent atrial fibrillation, not previously treated with therapeutic doses of antiarrhythmic drugs.

RAAFT Study – Patient Flow

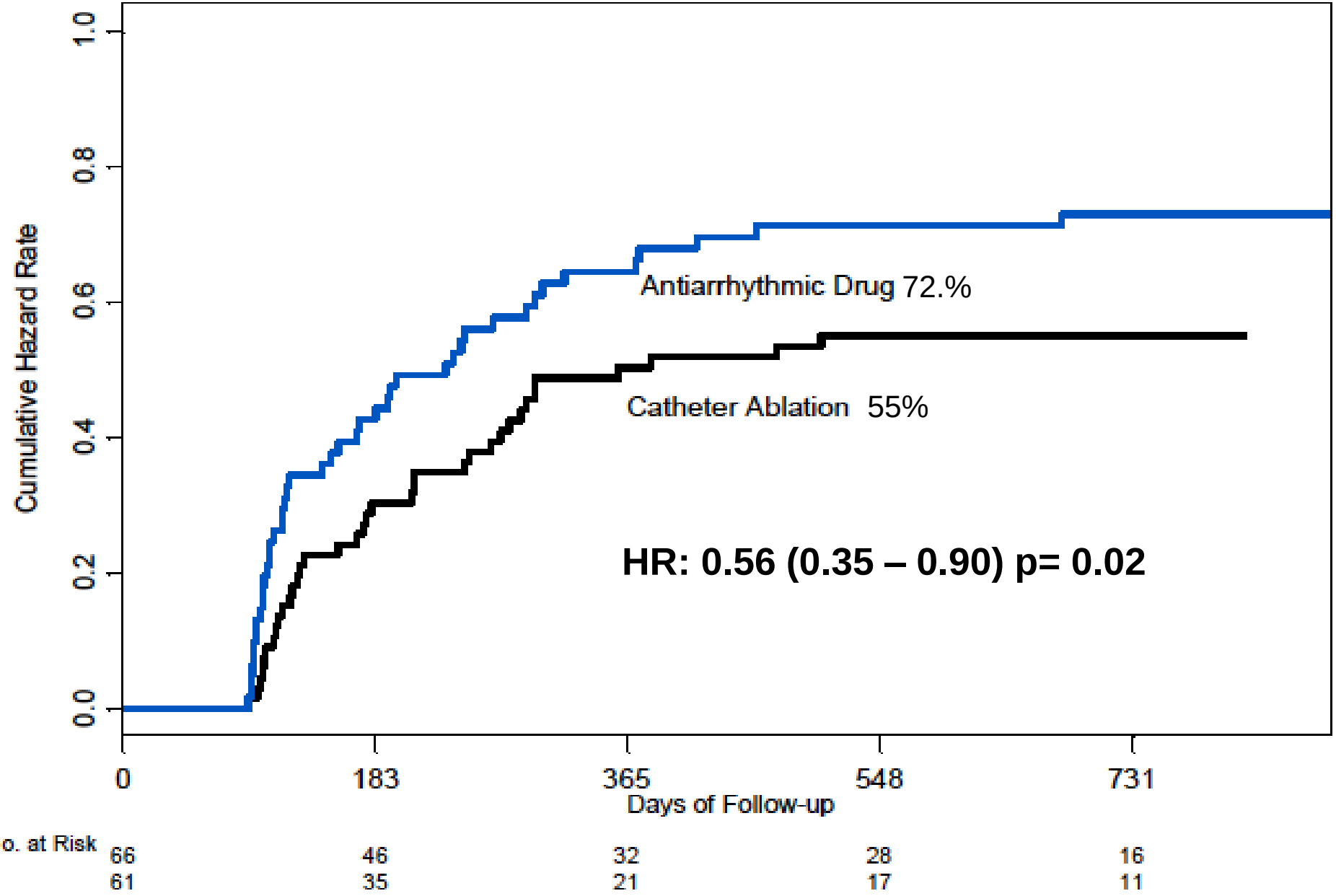


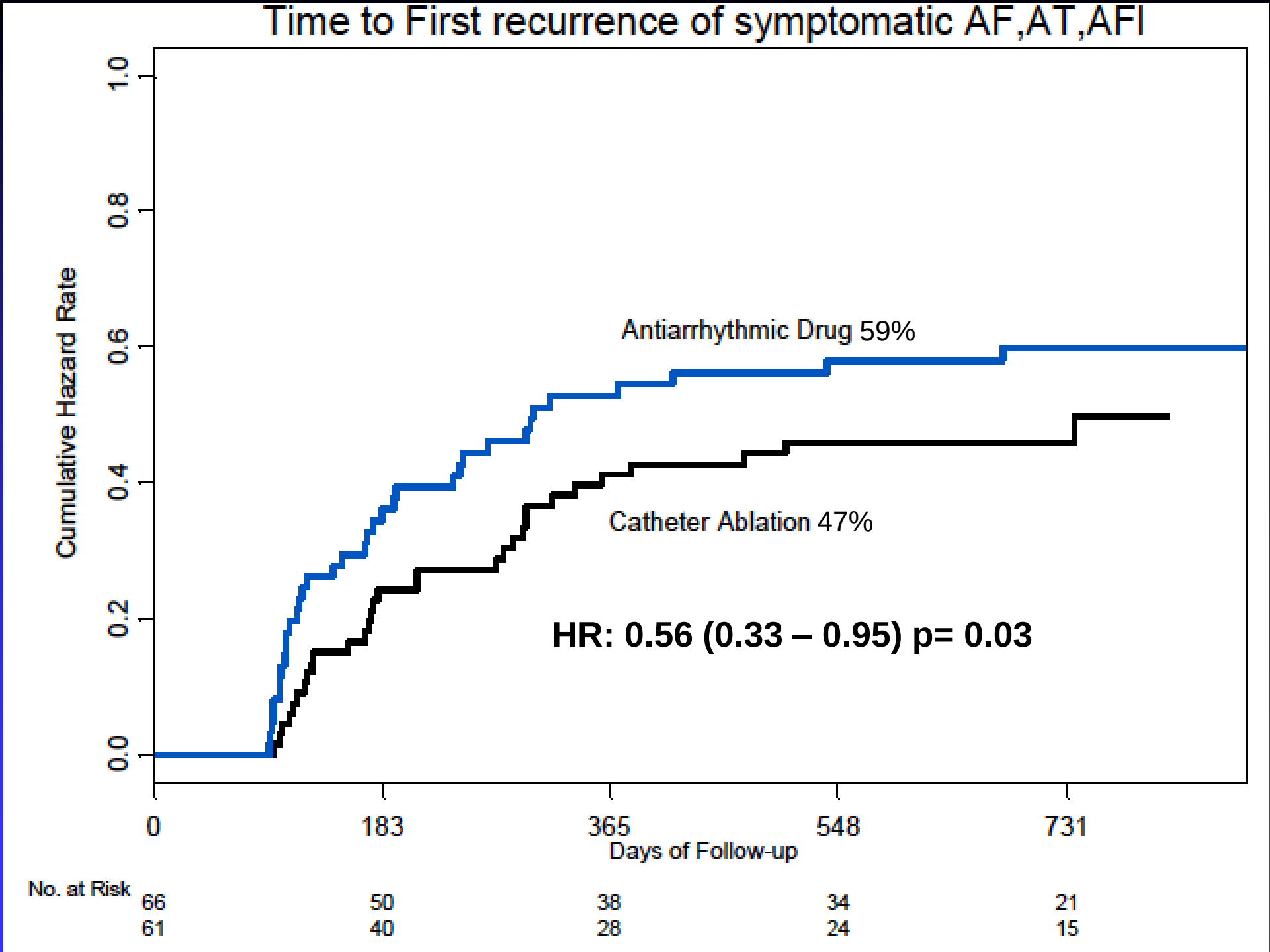
Baseline Characteristics

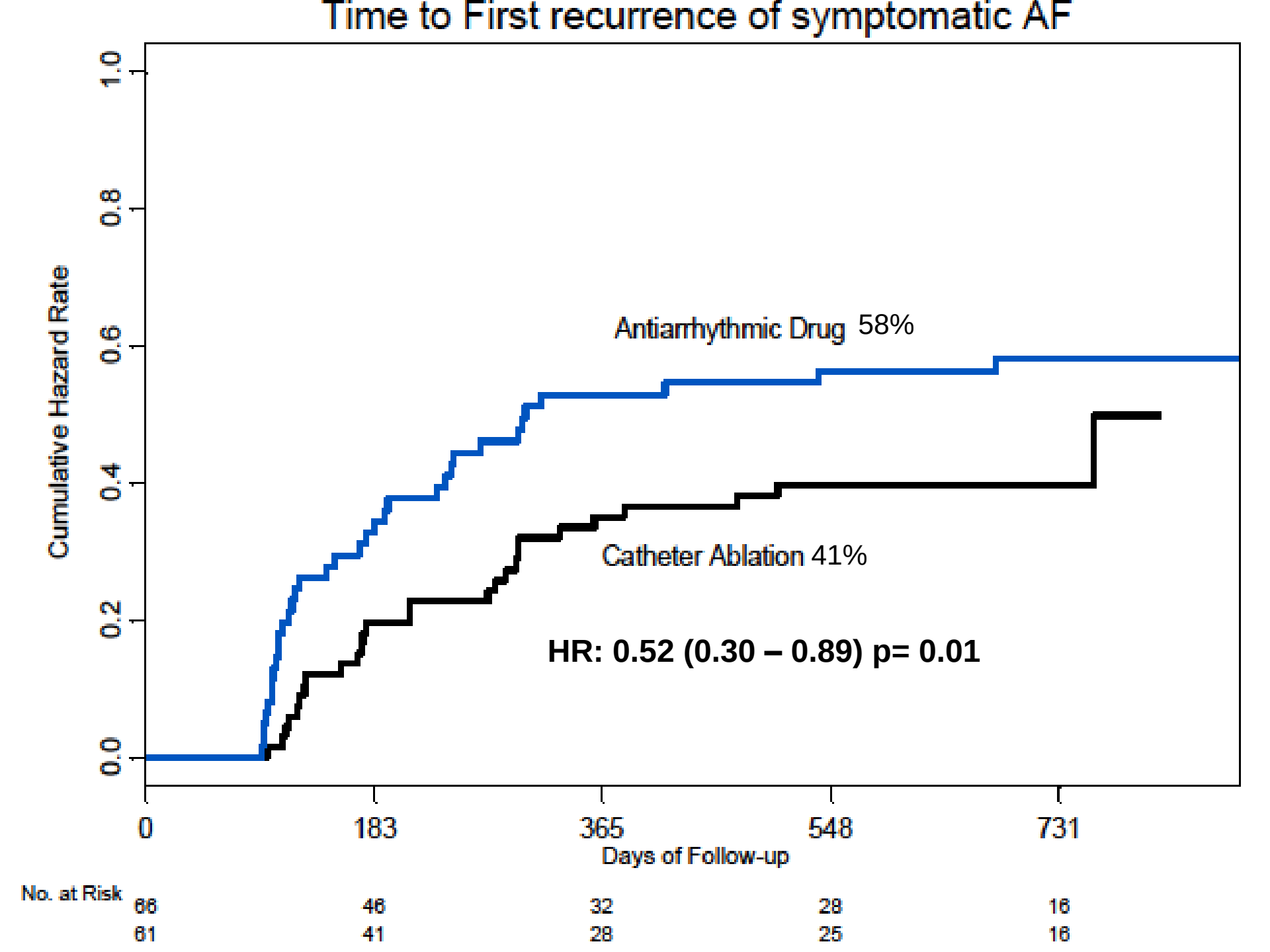
	PV Catheter Ablation	Antiarrhythmic Drug
Age, mean (SD)	56.3 (9.3)	54.3 (11.7)
Gender, Male	77.3%	73.8%
Paroxysmal AF	86.4%	88.5%
Persistent AF	13.6%	11.5%
Number of AF episodes past 6 months, mean (SD)	47.7 (97.9)	33 (48.7)
4 to 11 episodes in past 6 months	42.4%	44.3%
11 to 89 episodes in past 6 months	30.3%	31.1%
Previous Electrical Cardioversion	33.3%	52.5%

Primary Efficacy Outcome

Time to First recurrence of symptomatic/asymptomatic AF/AT/AFl




Time to First recurrence of symptomatic AF,AT,AFl
Cumulative Hazard Rate
0.0
0.2
0.4
0.6
0.8
1.0
Antiarrhythmic Drug 59%
Catheter Ablation 47%
HR: 0.56 (0.33 – 0.95) p= 0.03
0
183
365
548
731
Days of Follow-up
No. at Risk
66
50
38
34
21
61
40
28
24
15


Time to First recurrence of symptomatic AF
Cumulative Hazard Rate
0.0
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Antiarrhythmic Drug 58%
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0
183
365
548
731
Days of Follow-up
No. at Risk
66
46
32
28
16
61
41
28
25
16

Primary Safety Endpoint

Time to First Occurence	
Ablation Group	**AAD Group**
Death (0)	Death (0)
Cardiac Tamponade (6.2%)	Torsade de pointes (0)
Severe pulmonary vein stenosis $\geq$ 70% (1.5%)	Bradycardia leading to pacemaker insertion (0)
Atrio-esophageal fistula (0)	Syncope (3.3%)
Thromboembolism (Stroke, Non-CNS Embolism. (0)	QRS duration prolongation > 50% of baseline QRS duration (0)
Vascular complications (arterial pseudoaneurysm , arteriovenous fistula and hematoma leading to transfusion (0)	1:1 Atrial flutter (1.6%)
Phrenic nerve injury (0)	Any other significant adverse events that lead to ADT discontinuation. (14.3%)
Cluster : 7.7%	**Cluster: 19.7%**

Persistent Atrial Fibrillation

Catheter ablation vs. antiarrhythmic drug treatment of persistent atrial fibrillation: a multicentre, randomized, controlled trial (SARA study)

SARA

Symptomatic persistent AF

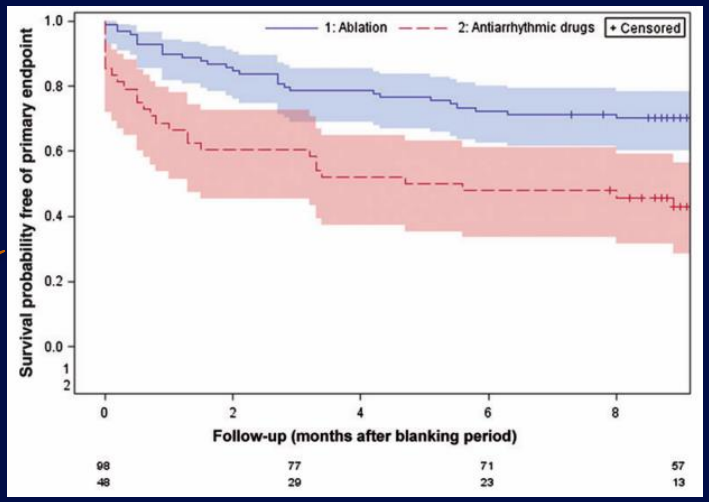
N = 146

PVAI (circumferential) ± lines (LA), CFAE

AAD (Ic or III)

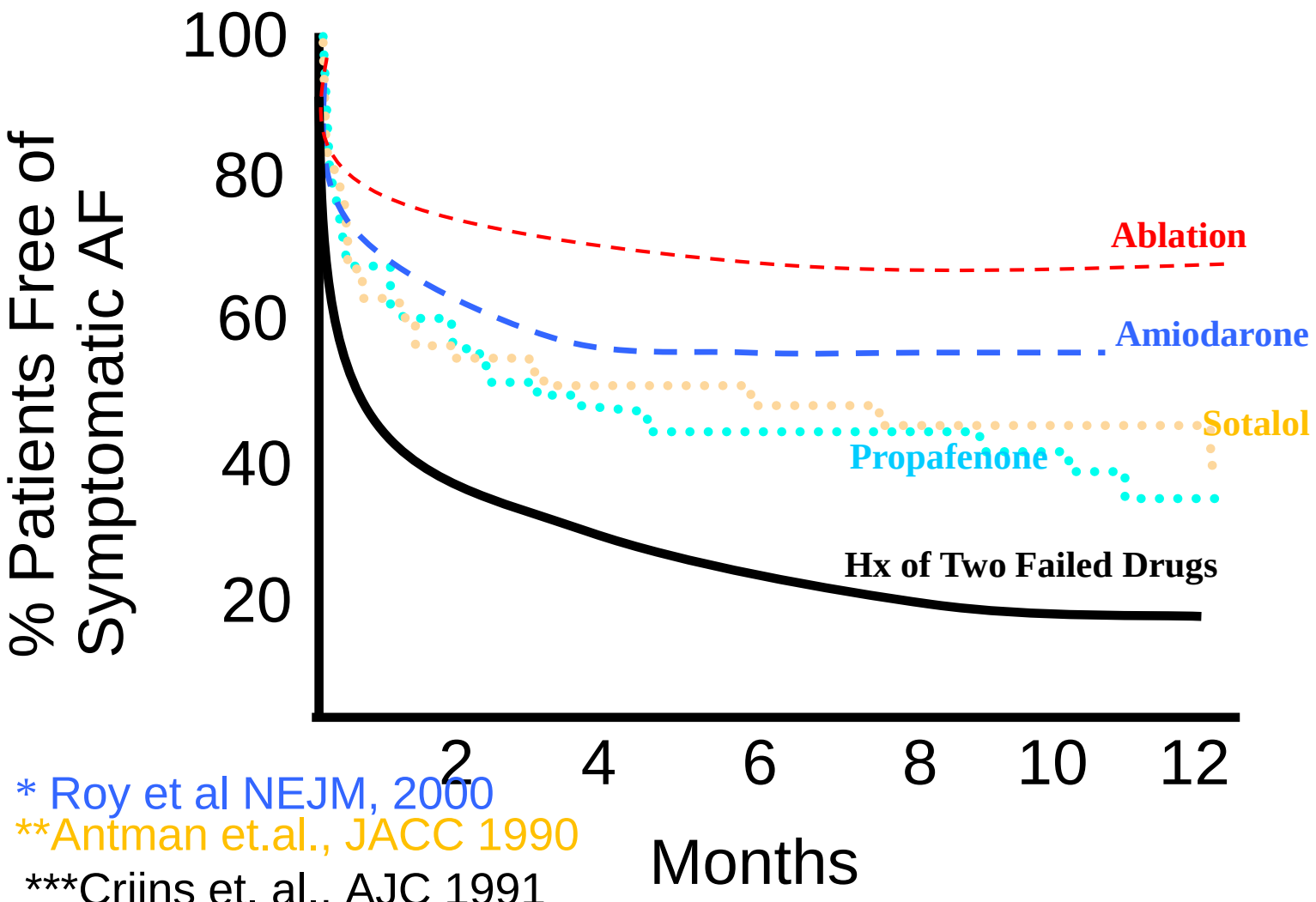
Freedom from AT/AF

FU = 12 months



70.4 vs 43.7 %
(p = 0.002)

Mont et al. Eur Heart J. 2014;35:501–7



* Roy et al NEJM, 2000
**Antman et.al., JACC 1990
***Crijns et. al., AJC 1991

Roy et al. NEJM. 2000. Antman et al. JACC 1990. Crijns et al. AJC 1991

Catheter ABlation vs ANtiarrhythmic Drug Therapy in Atrial Fibrillation (CABANA) Trial

Douglas L. Packer MD, Kerry L. Lee PhD,
Daniel B. Mark MD, MPH, Richard A. Robb PhD
for the CABANA Investigators

Mayo Clinic Rochester
Duke Clinical Research Institute
National Heart, Lung, and Blood Institute

MAYO CLINIC Duke Clinical Research Institute NIH National Heart, Lung, and Blood Institute

Purpose of CABANA

Compare Ablation to state-of-the-art drug therapy for patients with new onset / undertreated AF

Primary Endpoint

- **All-cause mortality, disabling stroke, serious bleeding, or cardiac arrest**

Major Secondary Endpoints

- **All-cause mortality**
- **Death (all-cause) or cardiovascular hospitalization**

CABANA Trial Design

Enroll patients with *new onset* or *under-treated* paroxysmal, persistent, or longstanding persistent AF who *warrant therapy*

Key Inclusion Criteria
- ≥65 years of age
- <65 years of age with ≥1 CVA/CV risk factor
- Eligible for ablation and
- ≥2 rhythm or rate control drugs

No Exclusion Criteria Identified

R
1:1

Ablation Therapy (1108)
Primary ablation:
- PVI/WACA

Ancillary ablation:
- Linear lesions
- CFAE

Anticoagulation

Drug Therapy (1096)
- Rate Control or
- Rhythm Control
- Anticoagulation

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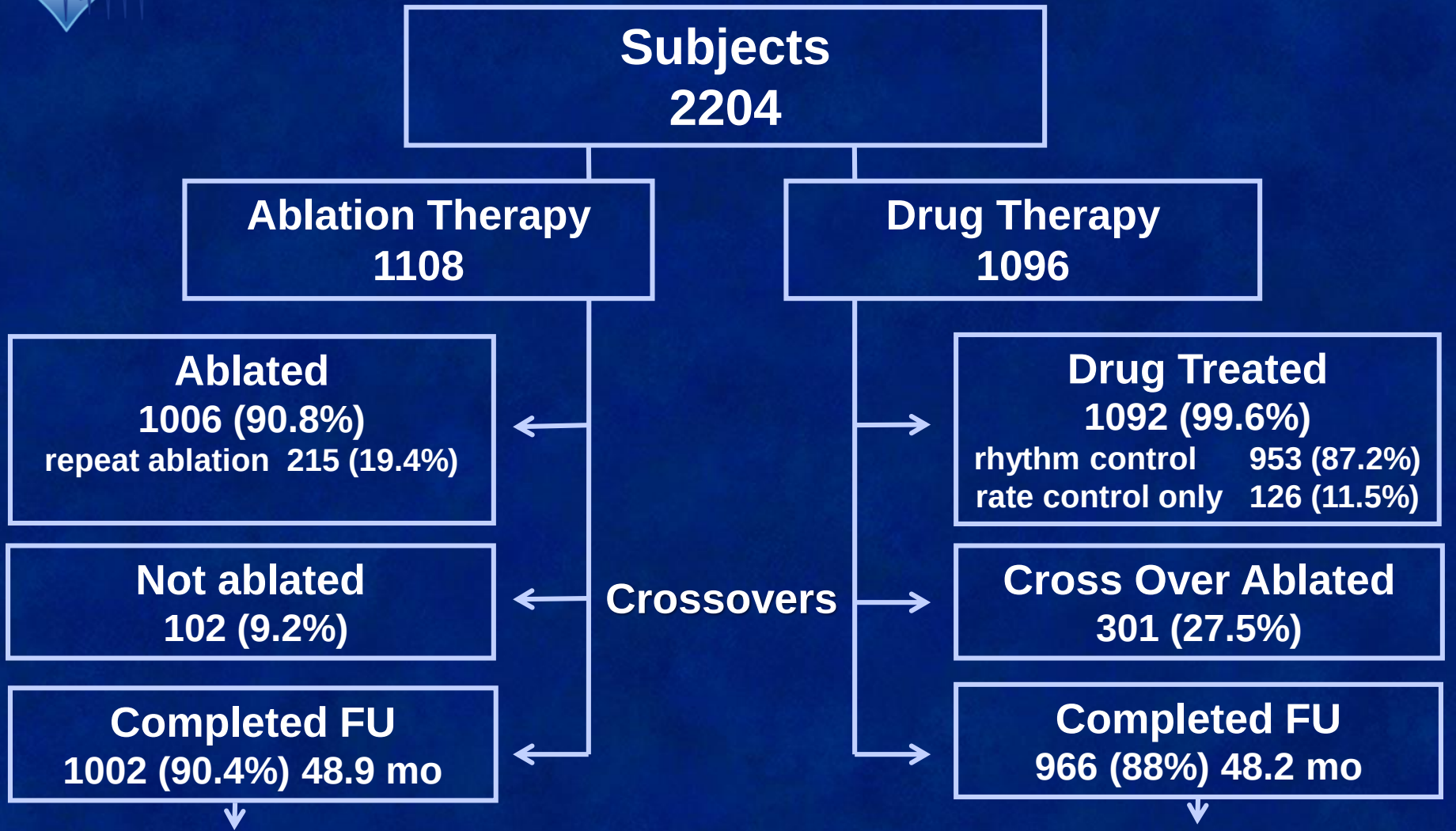
Patient Randomization



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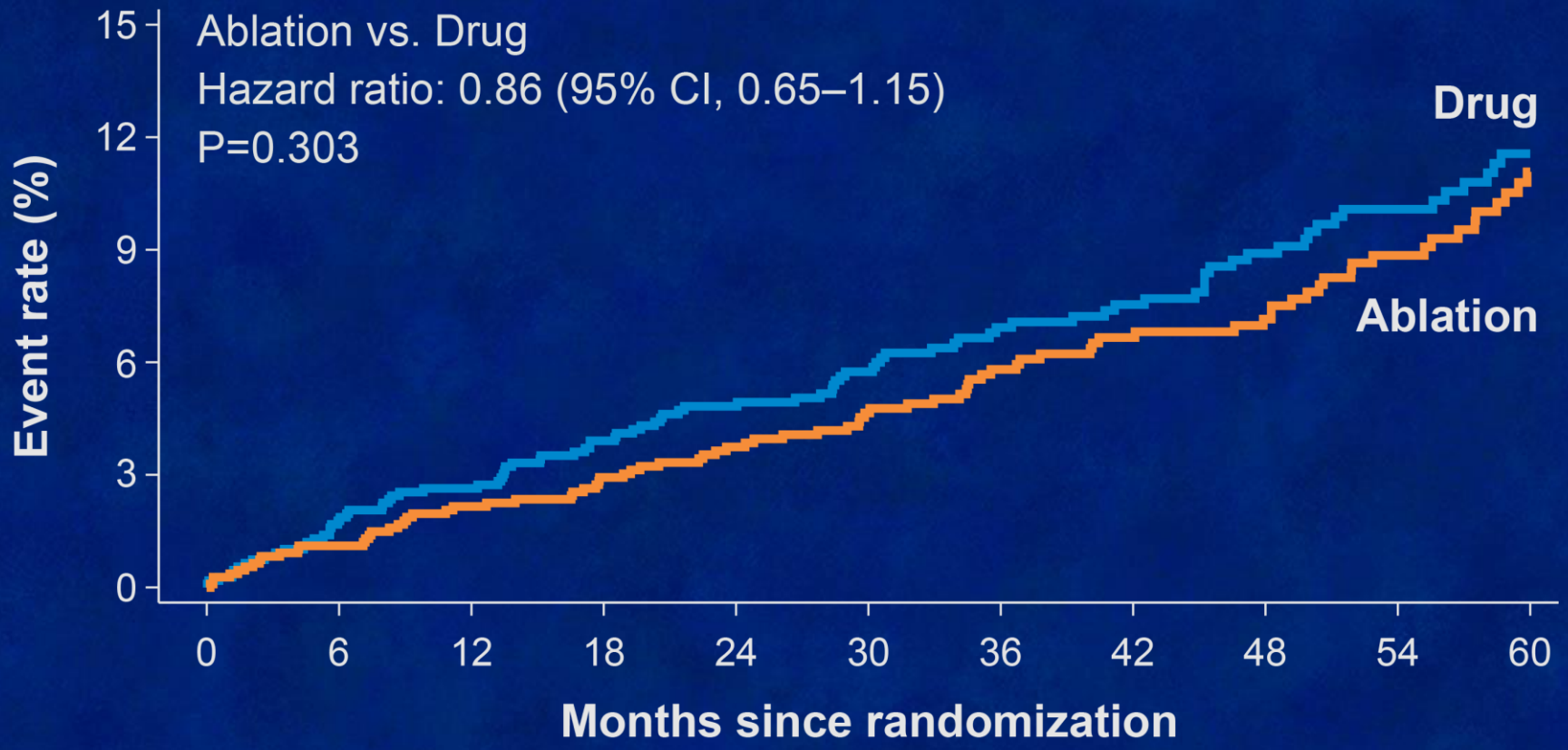
* Withdrew <3 years

Arrhythmia History in CABANA

AF Type	Ablation	Drug Therapy
Paroxysmal	42.4%	43.5%
Persistent	47.3%	47.3%
Longstanding Persistent	10.3%	9.2%
Years since onset of AF [Median (Q1,Q3)]	1.1 (0.3, 4.1	1.1 (0.3, 3.9)
CCS Severity of AF		
Class 0-1	34.6%	26.7%
Class 2	31.8%	32.4%
Class 3-4	43.5%	41.0%
Prior hospitalization for AF	40.6%	38.8%

Primary Endpoint (Death, Disabling Stroke, Serious Bleeding, or Cardiac Arrest) (ITT)



Number at risk

Drug	1096	1036	1006	970	880	763	652	578	499	418	312
Ablation	1108	1045	1021	996	915	793	700	614	535	432	309

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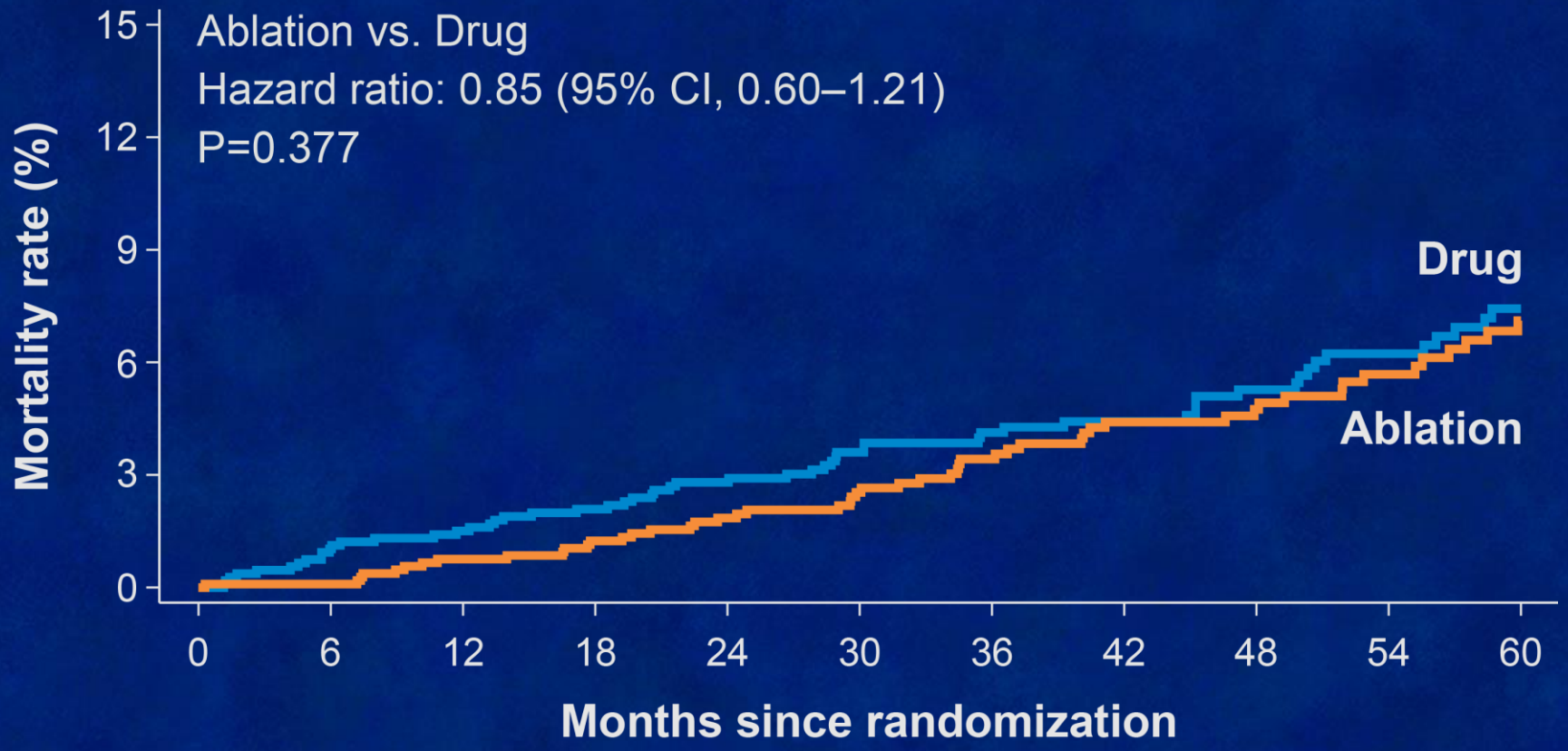
Estimates of All-Cause Mortality Risk (ITT)



Number at risk

Drug	1096	1046	1023	992	903	783	679	606	527	445	334
Ablation	1108	1058	1035	1013	933	814	724	632	555	455	332

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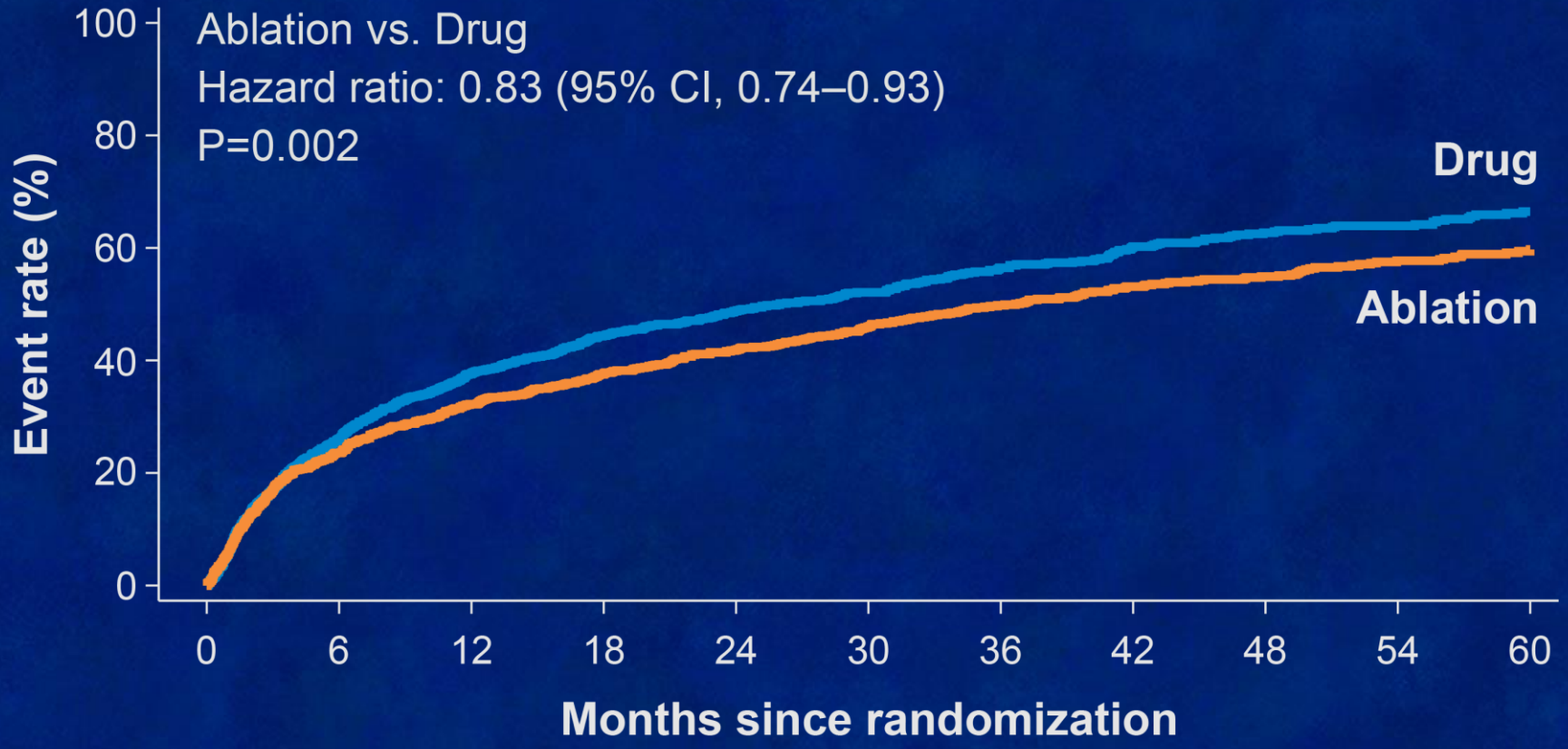
All-Cause Mortality or Cardiovascular Hospitalization (ITT)



Number at risk											
Drug	1096	778	643	563	474	387	302	244	197	165	112
Ablation	1108	807	708	643	558	450	372	307	261	207	137

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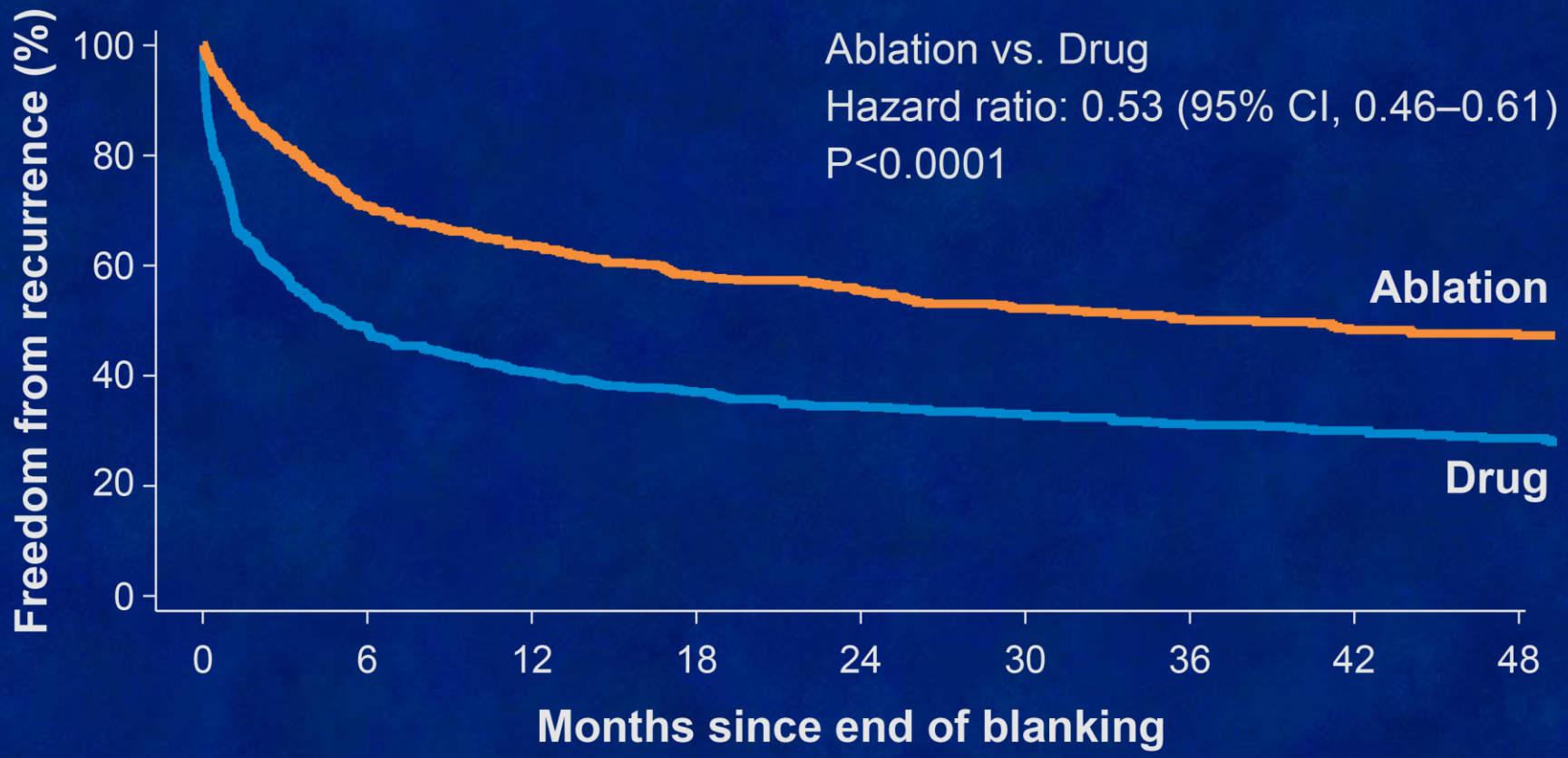
First Recurrence AF – Post Blanking* (ITT)



Number at risk									
Drug	629	303	251	211	180	156	130	114	93
Ablation	611	430	380	327	290	239	199	162	133

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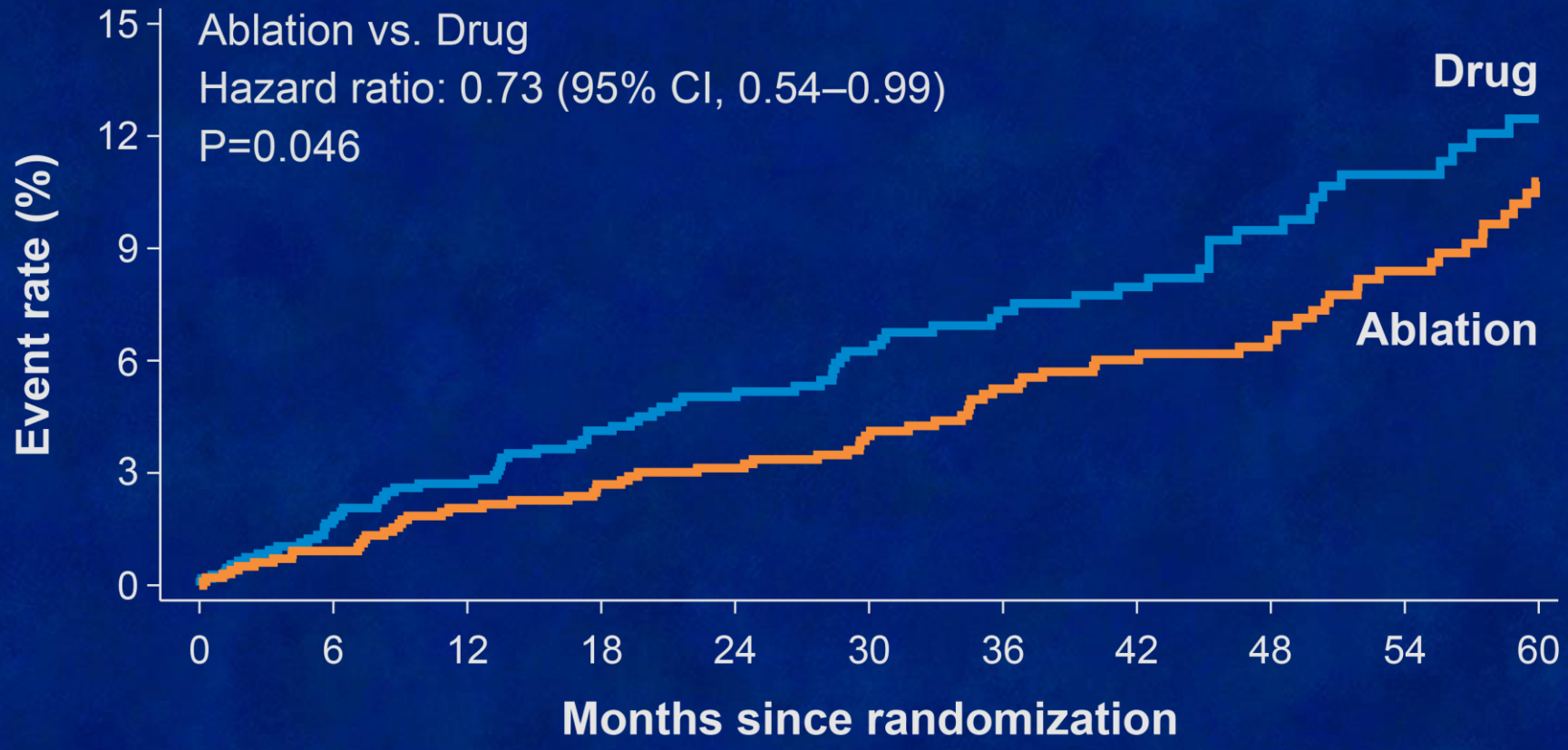
*Using CABANA Monitors

Primary and Secondary Outcomes (Treatment Received)*

	Ablation (N = 1307)	Drug (N = 897)	Hazard Ratio (95% CI)	P-Value
Primary Outcome	92 (7.0%)	98 (10.9%)	0.67 (0.50, 0.89)	0.006
Secondary Outcomes				
All-cause mortality	58 (4.4%)	67 (7.5%)	0.60 (0.42, 0.86)	0.005
Death or CV hospitalization	538 (41.2%)	672 (74.9%)	0.83 (0.74, 0.94)	0.002

*pre-specified

Primary Endpoint (Death, Disabling Stroke, Serious Bleeding, or Cardiac Arrest (Per Protocol)



Number at risk											
Drug	1096	954	860	778	680	566	464	396	330	275	204
Ablation	987	958	937	918	849	735	648	566	494	404	291

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Primary Endpoint Sub-group Analysis

All-Cause Mortality, Disabling Stroke, Serious Bleeding, Cardiac Arrest (Per Protocol)

Group	Interaction P-Value	N	Hazard Ratio	95% CI
All Subjects		2083	0.73	0.54, 0.99
Age	0.029			
< 65 years old		725	0.41	0.20, 0.85
≥ 65 and < 75 years old		1069	0.67	0.45, 1.01
≥ 75 years old		289	1.54	0.77, 3.08
Sex	0.159			
Male		1311	0.62	0.42, 0.91
Female		772	0.99	0.58, 1.68
Minority status	0.040			
White		1883	0.84	0.60, 1.17
Minority*		200	0.32	0.13, 0.75
AF type	0.719			
Paroxysmal		897	0.65	0.39, 1.08
Persistent		983	0.74	0.49, 1.14
Long-standing persistent		202	1.03	0.37, 2.86
Years since onset of AF	0.643			
≤ 1 year		1000	0.69	0.46, 1.04
> 1 year		1066	0.80	0.50, 1.30
Hypertension	0.805			
Absent		403	0.66	0.30, 1.49
Present		1679	0.74	0.53, 1.04
Hypertension with LVH	0.919			
Absent		1108	0.69	0.45, 1.05
Present		561	0.67	0.36, 1.22
Sleep apnea	0.350			
Absent		1598	0.80	0.55, 1.16
Present		484	0.58	0.32, 1.03
BMI	0.710			
< 30		1003	0.69	0.44, 1.06
≥ 30		1051	0.77	0.50, 1.20
CHADS-VASc score	0.928			
≤ 2		907	0.75	0.42, 1.32
> 2		1176	0.72	0.50, 1.05
History of congestive heart failure	0.147			
No		1772	0.84	0.59, 1.22
Yes		309	0.51	0.28, 0.91
Baseline NYHA class	0.198			
No heart failure or Class I		1327	0.89	0.58, 1.36
≥ Class II		740	0.59	0.37, 0.93

** Minority=Hispanic or Latino or non-white race*

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Adverse Events in CABANA

	Ablation n = 1006
Event	n (%)*
Catheter Insertion	39 (3.9)
Hematoma	23 (2.3)
Pseudo aneurysm	11 (1.1)
Atrial venous fistula	4 (0.4)
Pneumothorax	1 (0.1)
Sepsis	1 (0.1)
DVT	0
Pulmonary embolus	0
Catheter Manipulation Within the Heart	34 (3.4)
Pericardial effusion not requiring intervention	22 (2.2)
Cardiac tamponade with perforation	8 (0.8)
TIA	3 (0.3)
Coronary occlusion	0
Myocardial infarction	1 (0.1)
Complete heart block	0
Valvular damage	0
Ablation-related Events	18 (1.8)
Severe pericardial chest pain	11 (1.1)
Esophageal ulcer	5 (0.5)
Pulmonary Vein Stenosis > 75%	1 (0.1)
Phrenic nerve injury	1 (0.1)
Atrial esophageal fistula	0
Medication-related Events	0
Heparin induced bleeding	0

	Pts Receiving Drug n = 1092
Event	n (%)*
Hyper- or hypothyroidism	17 (1.6)
Hypotension	3 (0.3)
Major proarrhythmic event (VT,VF)	9 (0.8)
Torsades des pointes	0
Atrial proarrhythmic event	1 (0.1)
Heart failure	0
Allergic reaction	7 (0.6)
Gastrointestinal abnormality	3 (0.3)
Moderate or severe diarrhea	0
Liver injury/failure	3 (0.3)
Pulmonary toxicity	1 (0.1)
Blindness	0
Kidney damage	0
Renal failure	0
Severe headache	0

* n (%) = number (percent) of patients who reported drug-related adverse event. Percent is calculated among all patients that have received drug.

Quality of Life in the Catheter Ablation Versus Antiarrhythmic Drug Therapy for Atrial Fibrillation (CABANA) Trial

Daniel B. Mark, MD, MPH

Professor of Medicine
Vice Chief for Academic Affairs, Cardiology Division
Duke University Medical Center
Director, Outcomes Research
Duke Clinical Research Institute

Financial Disclosures

Consulting	Research Grants
CeleCor	NHLBI
	Eli Lilly & Company
	AstraZeneca
	Oxygen Therapeutics

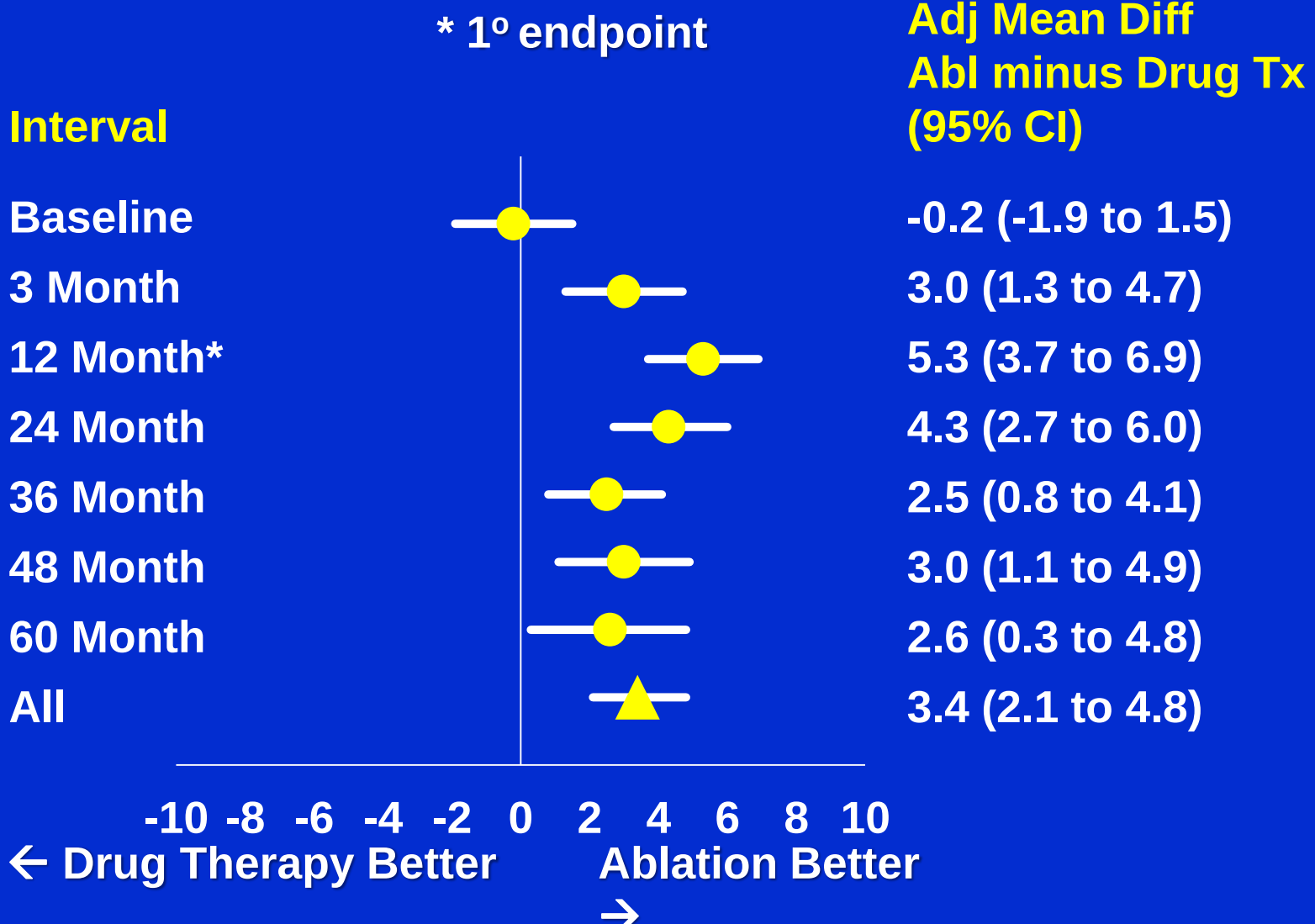
Co-Investigators/QOL Team

Kevin Anstrom
Shubin Sheng
Jonathan Piccini
Yves Rosenberg
Khaula Baloch
Melanie Daniels
Tristram Bahnson
J. David Knight
Jeanne Poole
Kerry Lee
Douglas Packer

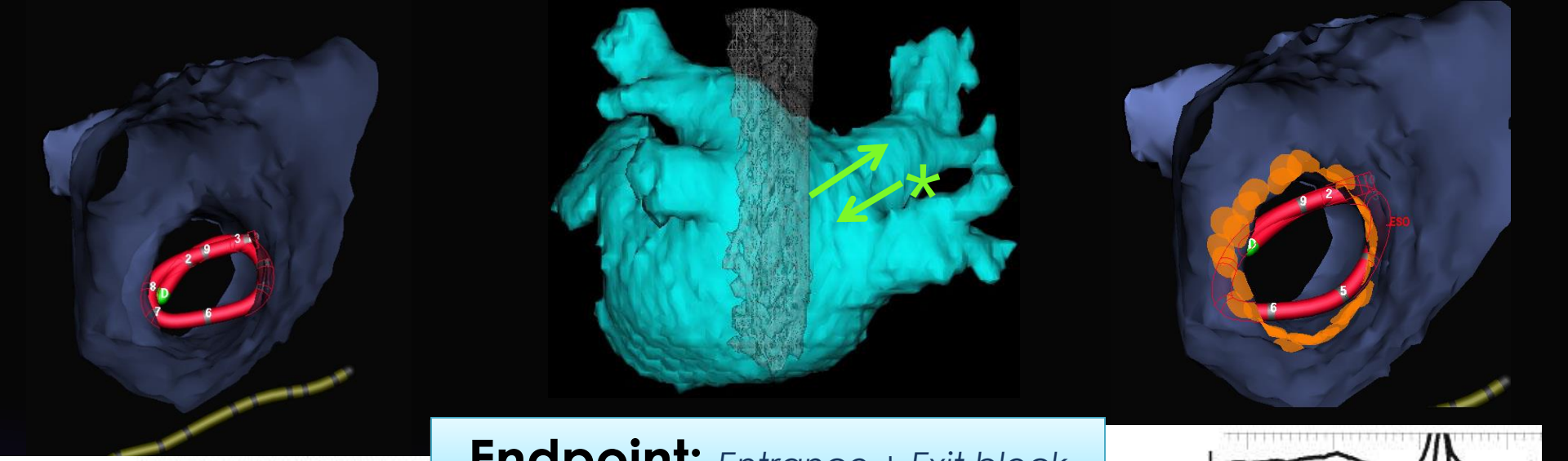
MAYO CLINIC | Duke Clinical Research Institute | NIH National Heart, Lung, and Blood Institute

August 26, 2018

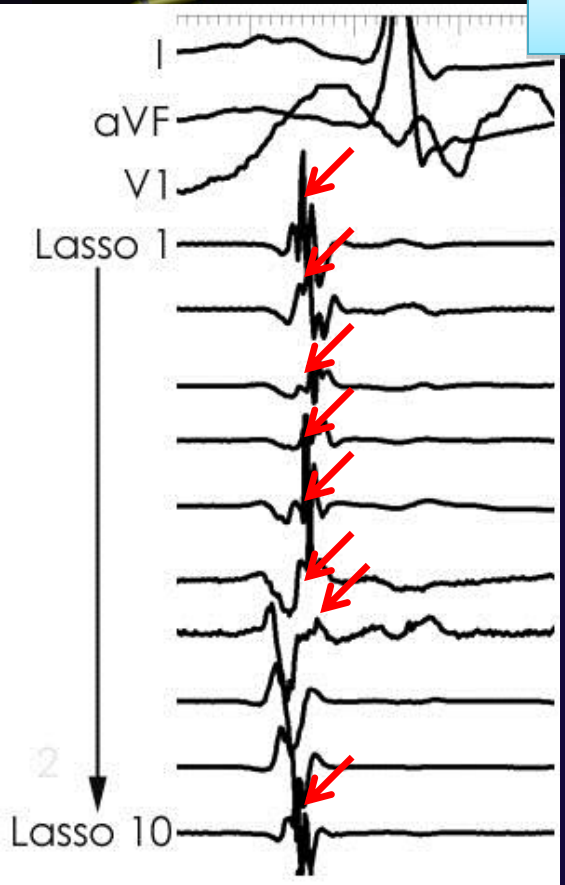
AFEQT Overall Score: Intention-to-Treat Analysis

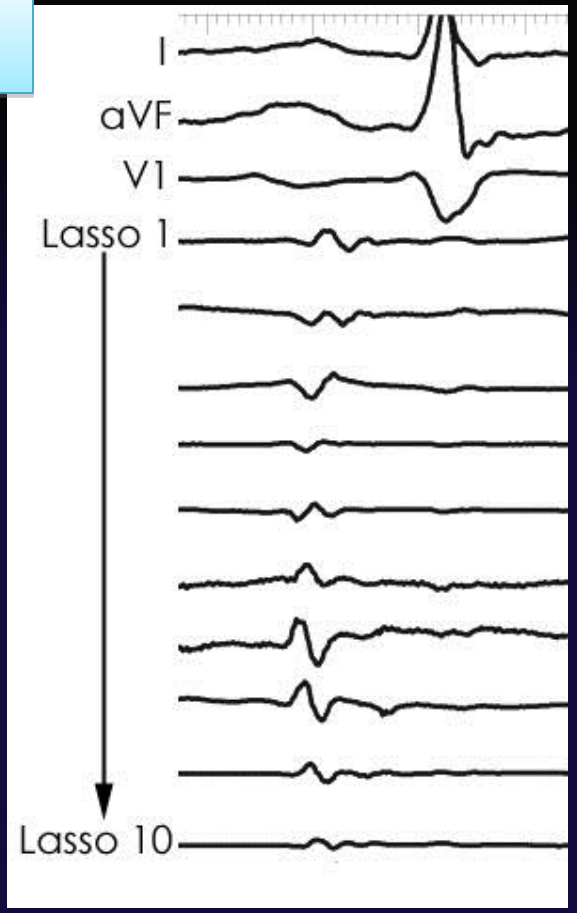


End Point Of Ablation



Endpoint: *Entrance + Exit block*

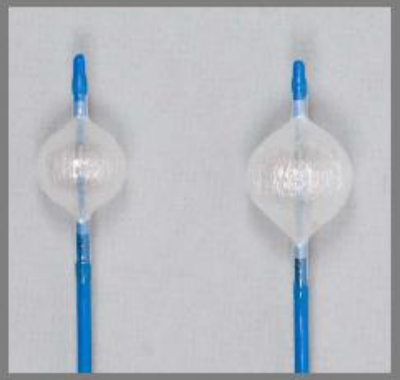




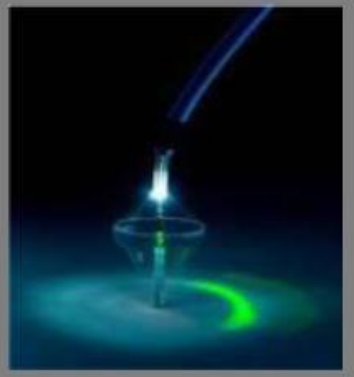
Pulmonary Vein Electrical Isolation

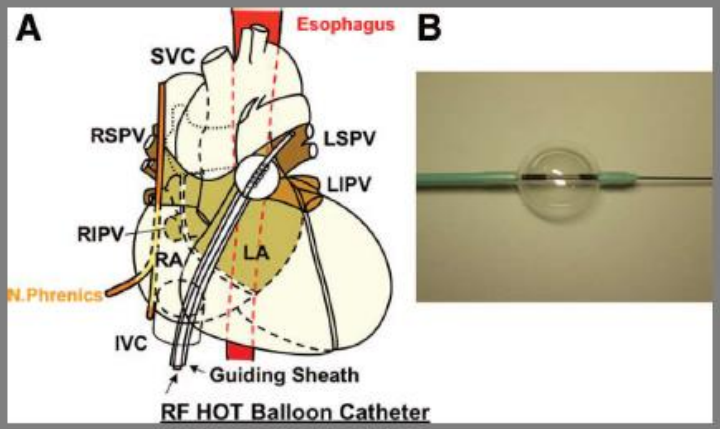
Current Status of Balloon Based Ablation Tools: where do they fit?

Arctic Front Cryoballoon

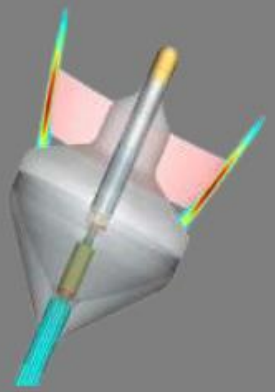


Laser Balloon





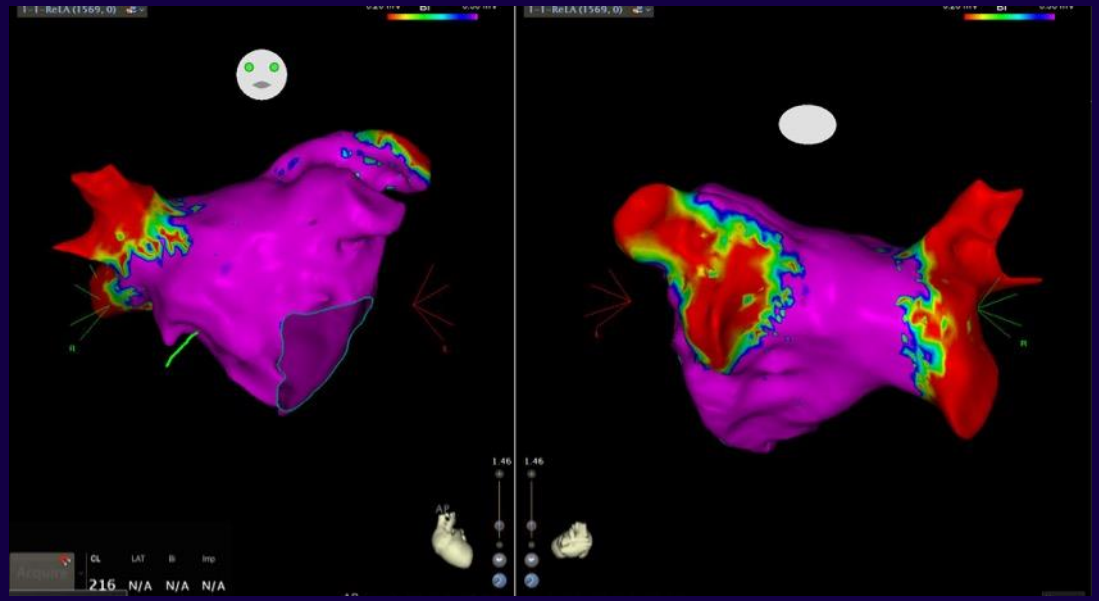
Toray Hot Balloon



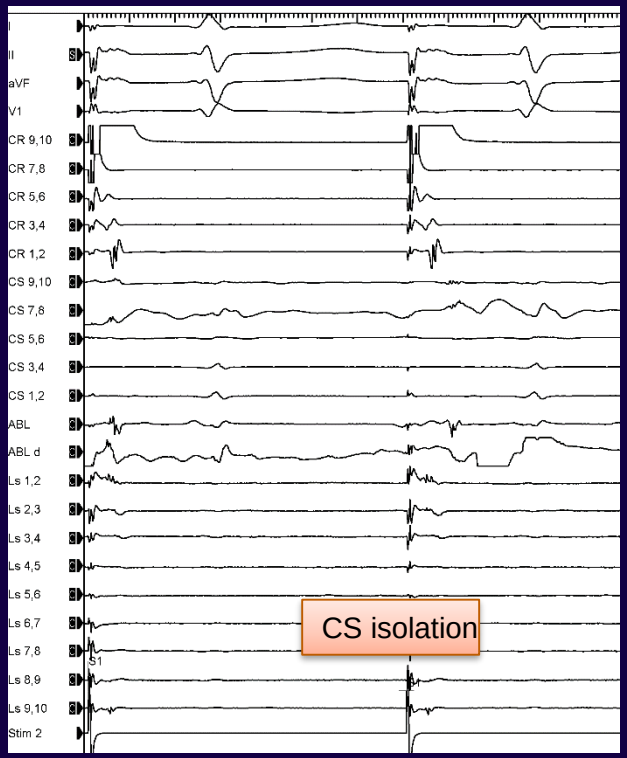
HIFU Balloon

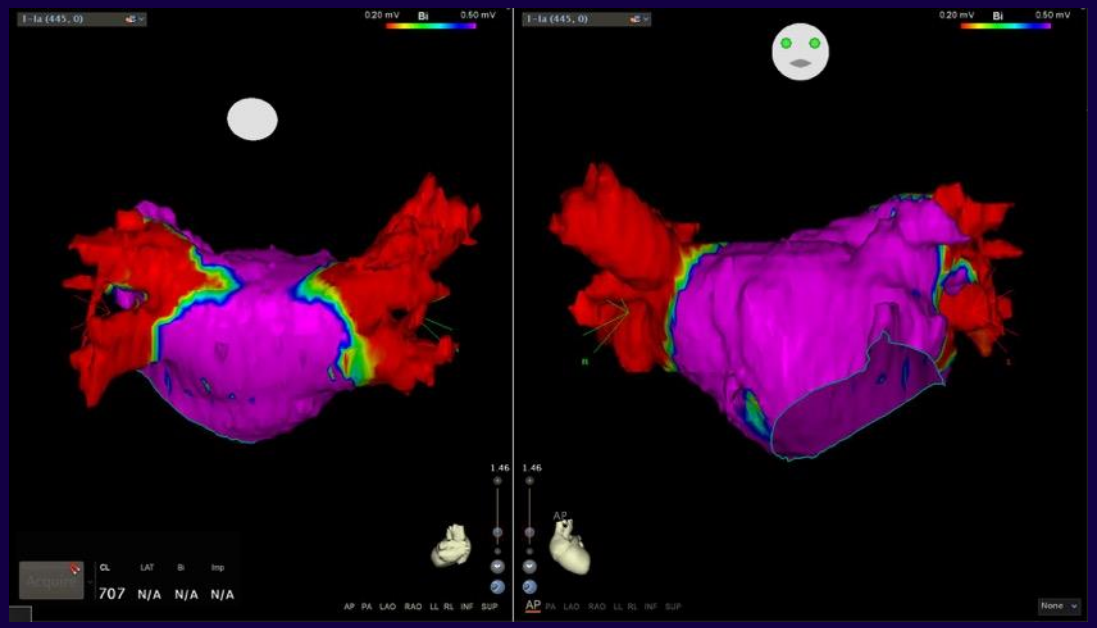
Ideal Patients

- Paroxysmal AF
- Short episode duration (4 to 8 hours)
- Minimal Structural heart problem
- No co-morbidity



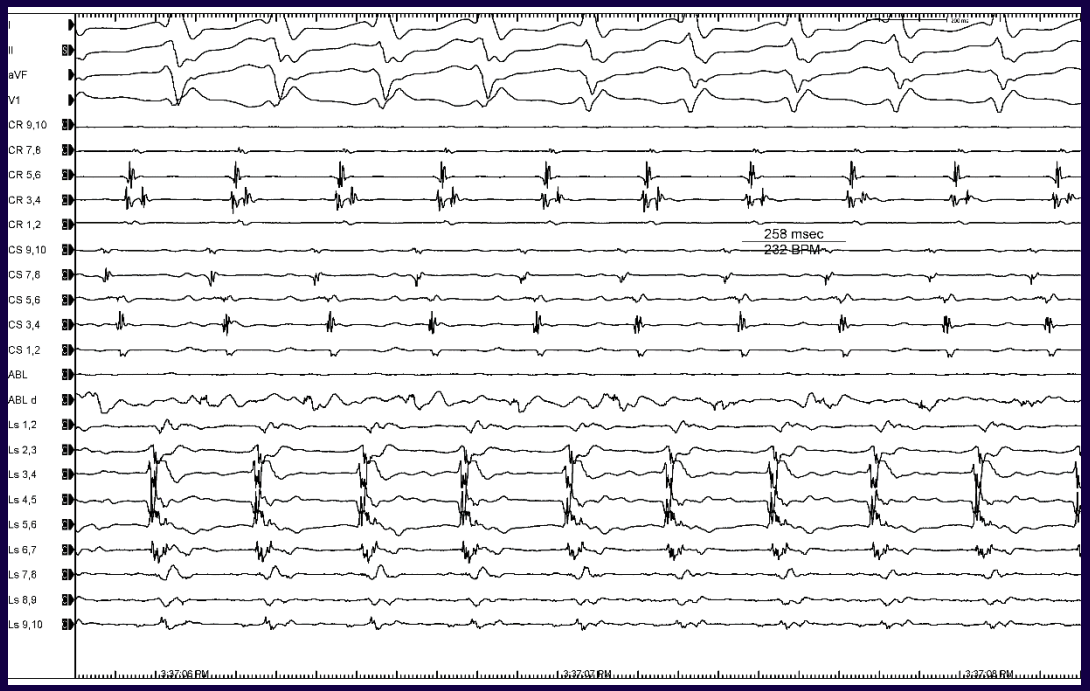
- 63 yo M
- drug refractory PAF
- 2 previous cryoablations
- late recurrence





- 67 yo M
- drug refractory PrAF
- 1 previous cryoablation
- recurrence

ISO 20 mcg/min



PULMONARY VEIN ANTRUM ISOLATION IN PATIENTS WITH PAROXYSMAL ATRIAL FIBRILLATION: MORE THAN A DECADE OF FOLLOW-UP

Natale et al. Circ Arrhyth 2016

Texas Cardiac Arrhythmia Institute, St. David's Medical Center, Austin (TX)
California Pacific Medical Center, San Francisco (CA)

Original Article

Pulmonary Vein Antrum Isolation in Patients With Paroxysmal Atrial Fibrillation

More Than a Decade of Follow-Up

Yalçın Gökoğlan, MD; Sanghamitra Mohanty, MD, MS, FHRS; Mahmut F. Güneş, MD; Chintan Trivedi, MD, MPH; Pasquale Santangeli, MD; Carola Gianni, MD; Issa K. Asfour, BS; Rong Bai, MD, FHRS; J. David Burkhardt, MD, FHRS; Rodney Horton, MD, FHRS; Javier Sanchez, MD; Steven Hao, MD; Richard Hongo, MD; Salwa Beheiry, RN; Luigi Di Biase, MD, PhD, FHRS; Andrea Natale, MD, FHRS, FESC

Background—We report the outcome of pulmonary vein (PV) antrum isolation in paroxysmal atrial fibrillation (AF) patients over more than a decade of follow-up.

Methods and Results—A total of 513 paroxysmal AF patients (age 54±11 years, 73% males) undergoing catheter ablation at our institutions were included in this analysis. PV antrum isolation extended to the posterior wall between PVs plus empirical isolation of the superior vena cava was performed in all. Non-PV triggers were targeted during repeat procedure(s). Follow-up was performed quarterly for the first year and every 6 to 9 months thereafter. The outcome of this study was freedom from recurrent AF/atrial tachycardia. At 12 years, single-procedure arrhythmia-free survival was achieved in 58.7% of patients. Overall, the rate of recurrent arrhythmia (AF/atrial tachycardia) was 21% at 1 year, 11% between 1 and 3 years, 4% between 3 and 6 years, and 5.3% between 6 and 12 years. Repeat procedure was performed in 74% of patients. Reconnection in the PV antrum was found in 31% of patients after a single procedure and in no patients after 2 procedures. Non-PV triggers were found and targeted in all patients presenting with recurrent arrhythmia after ≥2 procedures. At 12 years, after multiple procedures, freedom from recurrent AF/atrial tachycardia was achieved in 87%.

Conclusions—In patients with paroxysmal AF undergoing extended PV antrum isolation, the rate of late recurrence is lower than what previously reported with segmental or less extensive antral isolation. However, over more than a decade of follow-up, nearly 14% of patients developed recurrence because of new non-PV triggers. **(*Circ Arrhythm Electrophysiol.* 2016;9:e003660. DOI: 10.1161/CIRCEP.115.003660.)**

Key Words: atrial fibrillation ■ non-PV triggers ■ paroxysmal AF ■ pulmonary vein isolation ■ recurrence

Atrial fibrillation (AF) is the most common sustained arrhythmia associated with a variety of adverse outcomes, including death, stroke, heart failure, reduced quality of life, and increased rate of hospitalizations.[1] Because the initial observation of pulmonary veins (PV) triggering AF was described by Haissaguerre et al[2] in 1998, significant advances have been made in the catheter-based treatment of AF. Today, pulmonary vein antrum isolation (PVAI) is the cornerstone of catheter-based therapies in symptomatic, drug-resistant paroxysmal AF (PAF) patients.

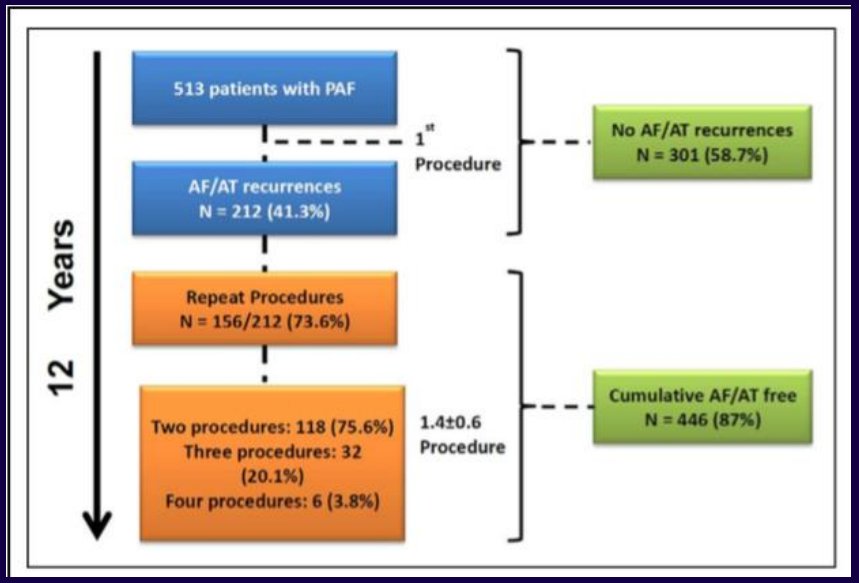
See Editorial by Kumar and Michaud

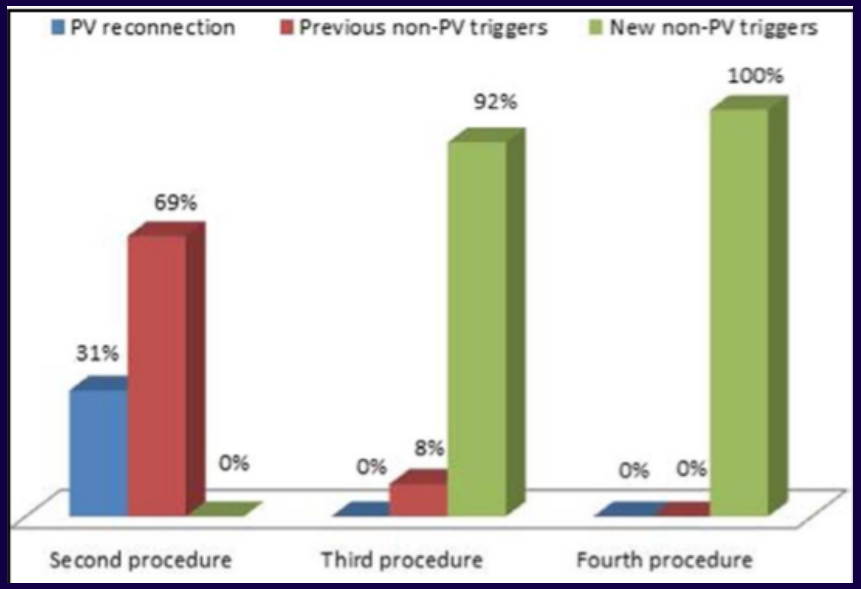
Long-term arrhythmia-free survival after AF ablation is important and highly desirable because this would have beneficial effects on patient prognosis, clinical decision-making process, and economic policies. Long-term success is defined as freedom from AF/atrial flutter (AFL)/atrial tachycardia (AT) recurrences after the 3-month blanking period through a minimum of 36-month follow-up from the date of the ablation procedure in the absence of Class I and III antiarrhythmic drug (AAD) therapy according to the latest guidelines.[3] Several published reports have provided information on the outcomes of AF ablation.[4–20] A meta-analysis evaluating studies reporting >3 years of outcome after catheter ablation (CA) found that nearly 80% multiprocedure success rates can be achieved in patients with PAF.[21]

Few series have reported long-term outcomes of AF ablation over 5 years.[4,6–10,12–16] However, data on long-term follow-up of PVAI are limited, which would provide valuable information regarding the efficacy and safety of CA and necessity of repeat procedures. Therefore, we sought to assess the outcome of PVAI in patients with PAF over a follow-up period of more than a decade.

Received October 8, 2015; accepted March 1, 2016.
For the author affiliations, please see the Appendix section.
Correspondence to Andrea Natale, MD, Texas Cardiac Arrhythmia Institute, St David's Medical Center, 3000 N IH-35, Suite 720, Austin, TX 78705. E-mail dr.natale@gmail.com

Variable	Number of Patients (N=513)
Demographics	
Male	374 (73%)
Age	54.4±10.6
BMI, kg/m^2	28.0±5.2
BMI ≥30 kg/m^2	176 (34.3)
Duration of AF	48 (24, 80.5)
Comorbidities	
Hypertension	180 (35.1)
Diabetes mellitus	41 (8.0)
Dyslipidemia	228 (44.4)
CAD	85 (16.6)
History of Stroke/TIA	13 (2.5)
COPD	8 (1.6)
Sleep apnea	37 (7.2)
Preprocedure echo parameters	
LAD, cm	4.3±0.6
LVEF, %	54.4±7.6
Procedural parameters	
Procedure time, min	137.3±55.5
Fluoroscopic time, min	43.7±21.5
Radiofrequency time, min	57.1±24.3
Presence of scar	125 (24.4%)
Cardioversion during the procedure	64 (12.5%)
Baseline INR	1.9±0.5





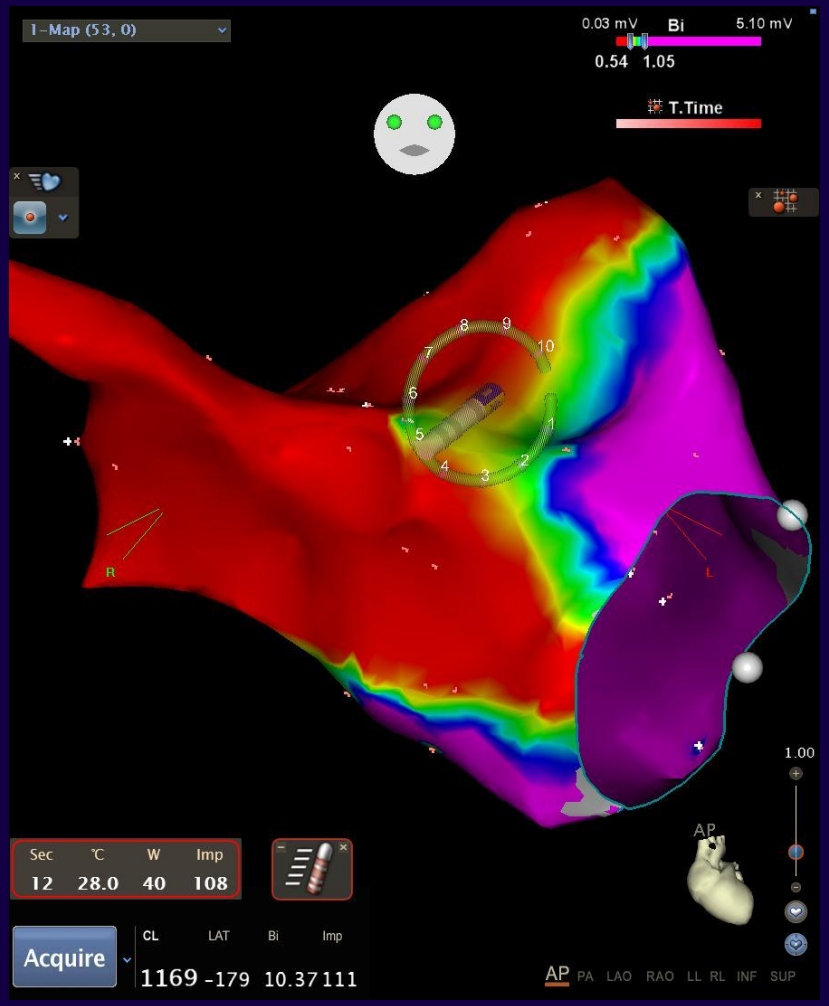
Circ Arrhythm Electrophysiol 2016;9:e003660

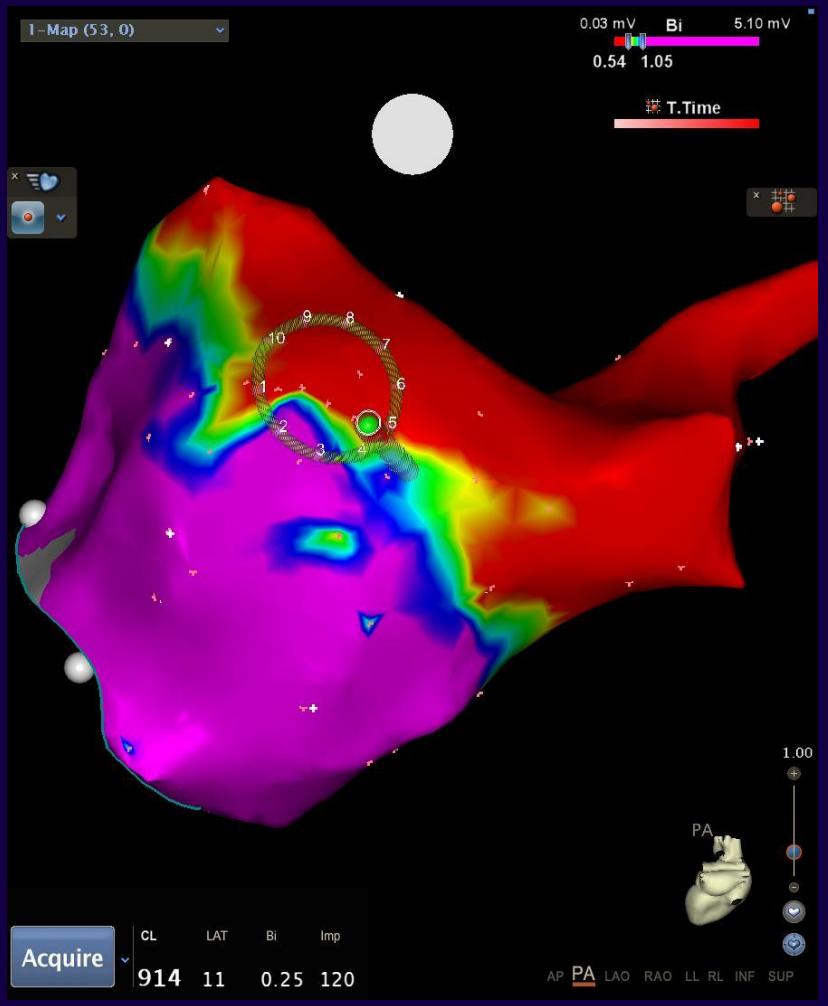
Patient History

- Female patient now 84 year old who had and ablation for paroxysmal atrial fibrillation 12 years ago and did well till a few months ago when she experienced recurrences of atrial arrhythmias requiring cardioversion
- She was considered for a repeat procedure

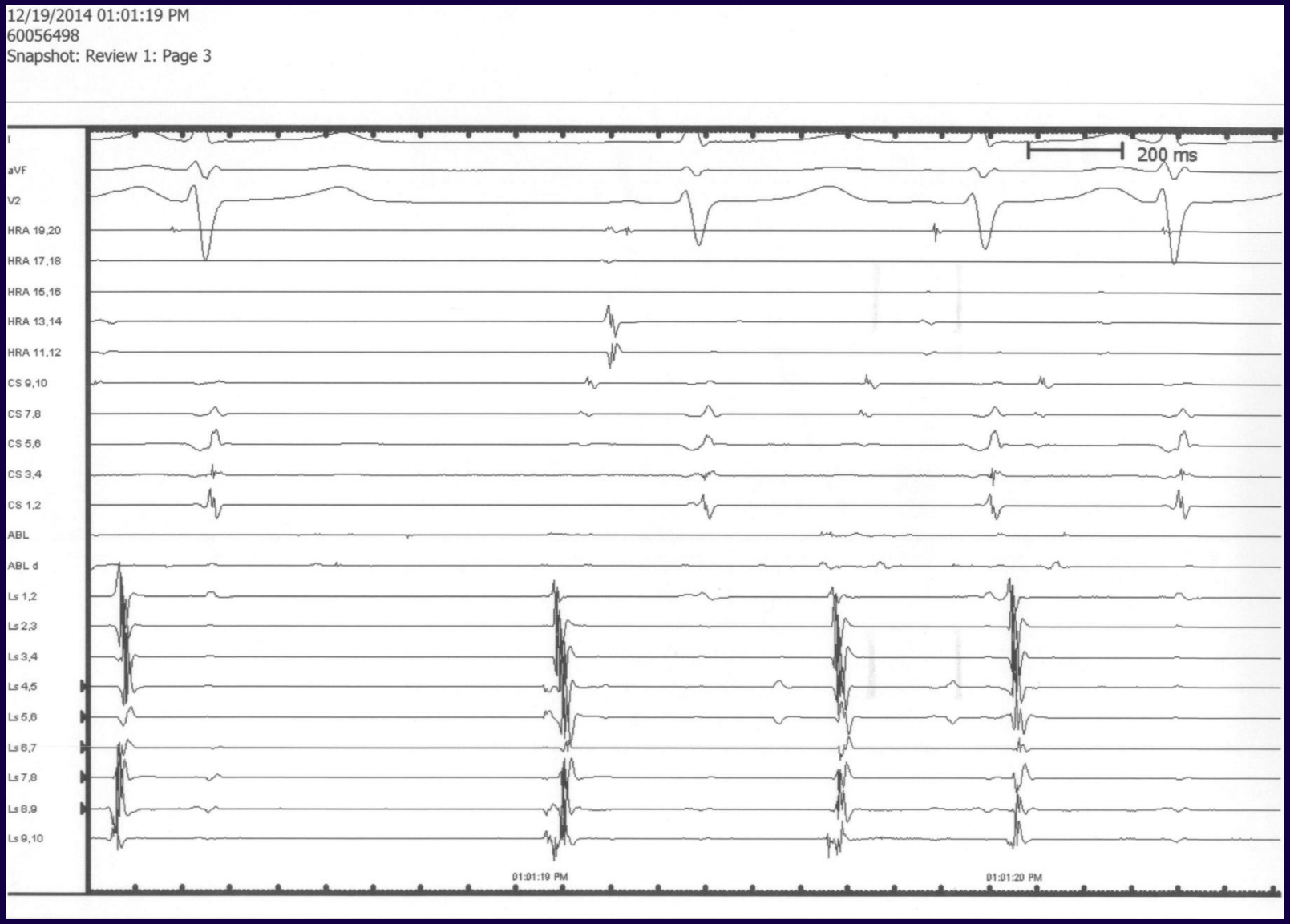
CASE 1

Voltage Map





CASE 1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aVF
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HRA 19,20
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HRA 11,12
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CS 5,6
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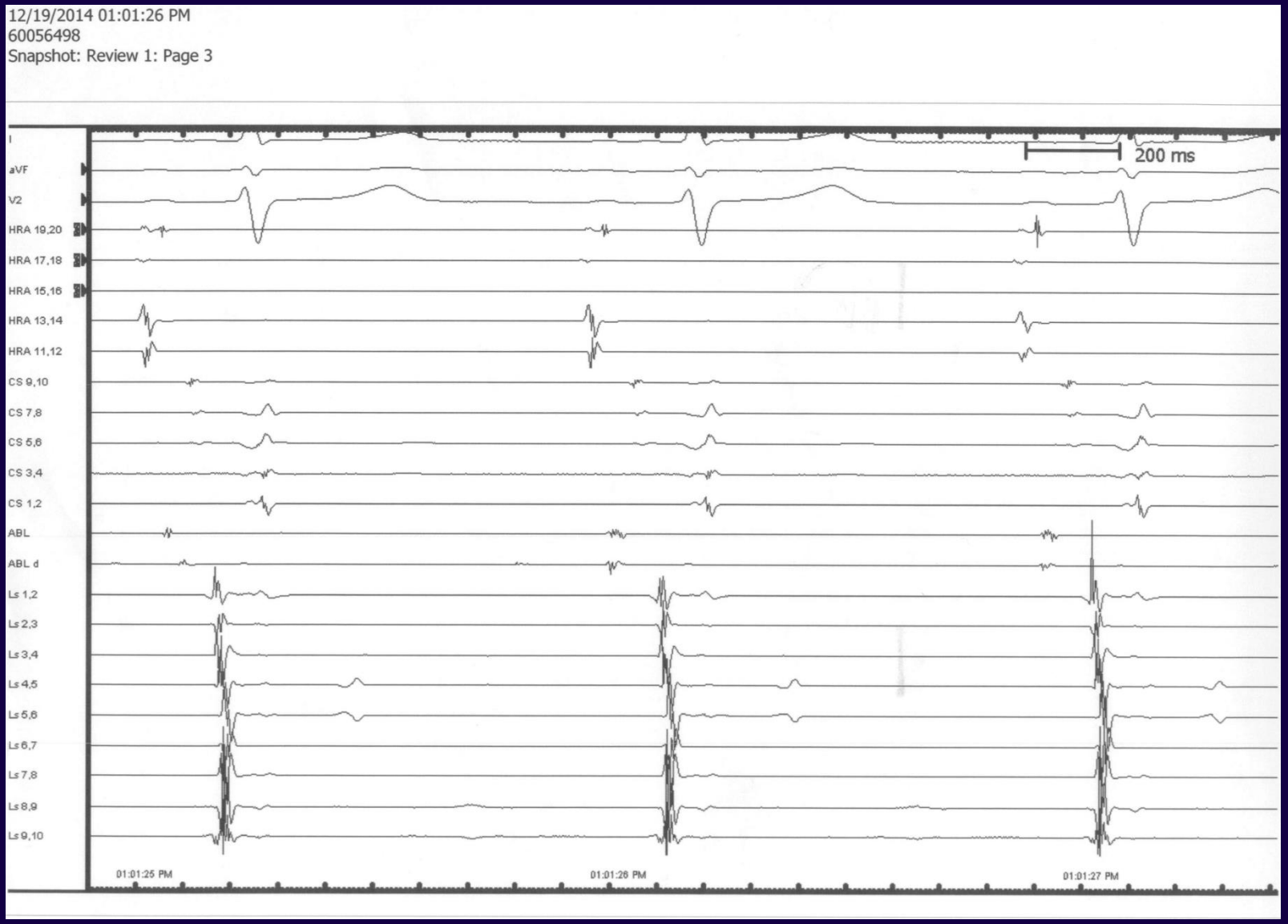
CASE 1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HRA 19,20
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CS 9,10
CS 7,8
CS 5,6
CS 3,4
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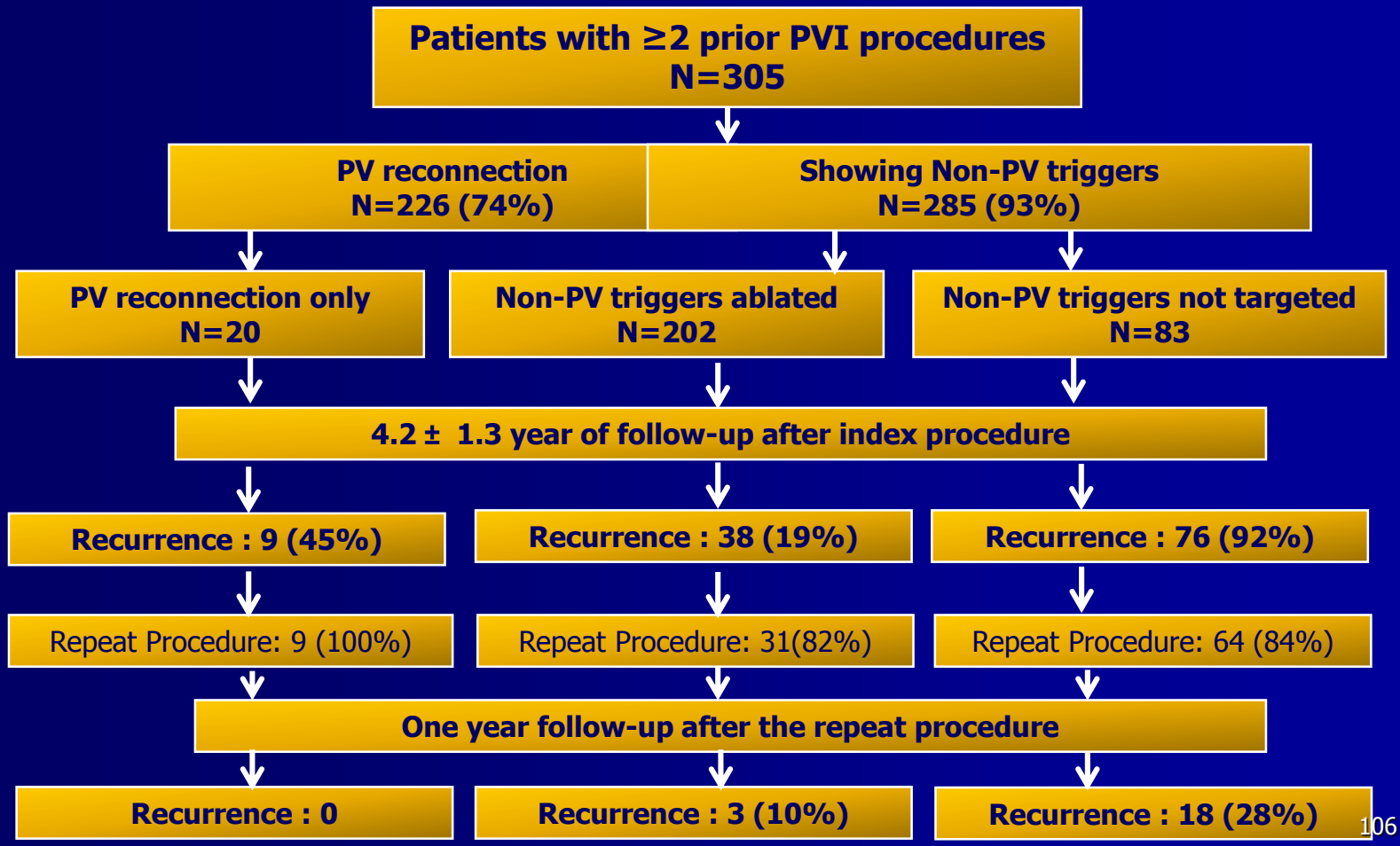
Groups With Higher Prevalence of Non PV Triggers

- Severe left atrial scarring
- Non paroxysmal AF
- Females
- Sleep apnea/obesity
- LV dysfunction
- Valve surgery
- Hypertrophic Cardiomyopathy
- Older Age

Procedural findings and ablation outcome in patients with atrial fibrillation referred after two or more failed catheter ablations

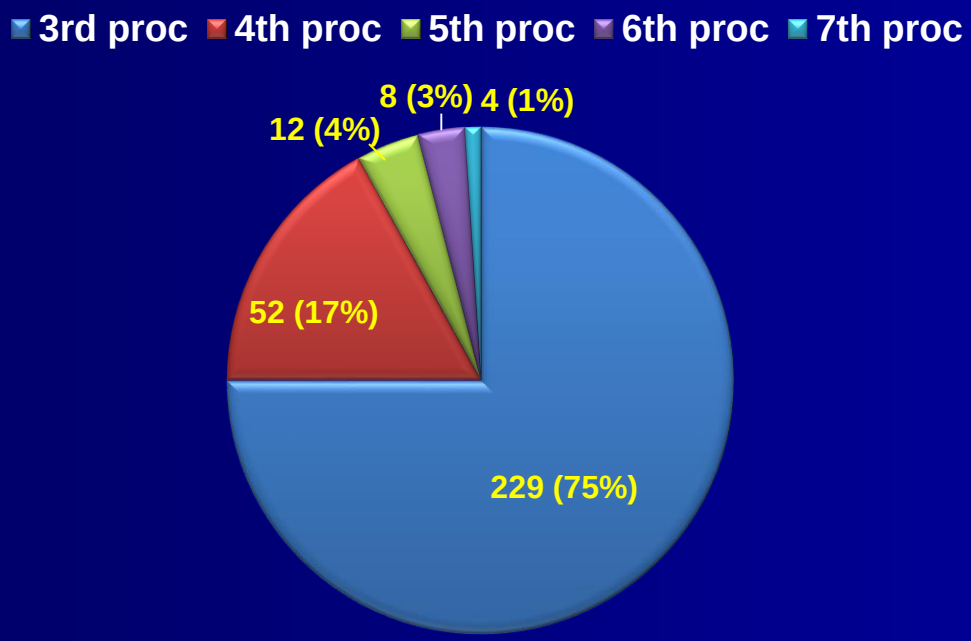
JCE 2018

Study Design:

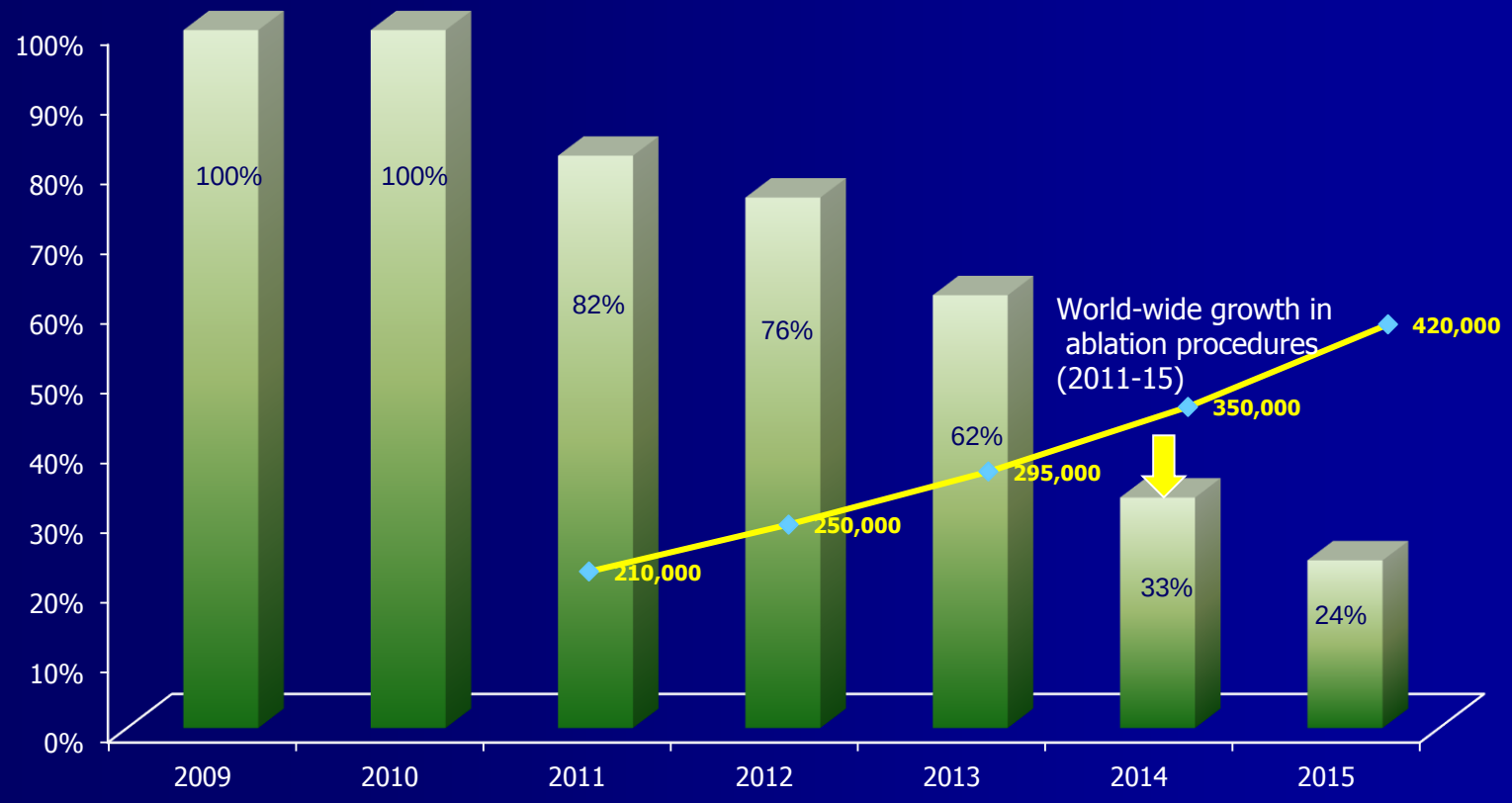


Study Population:

- N = 305
- Number of prior procedures: 2.4±0.8



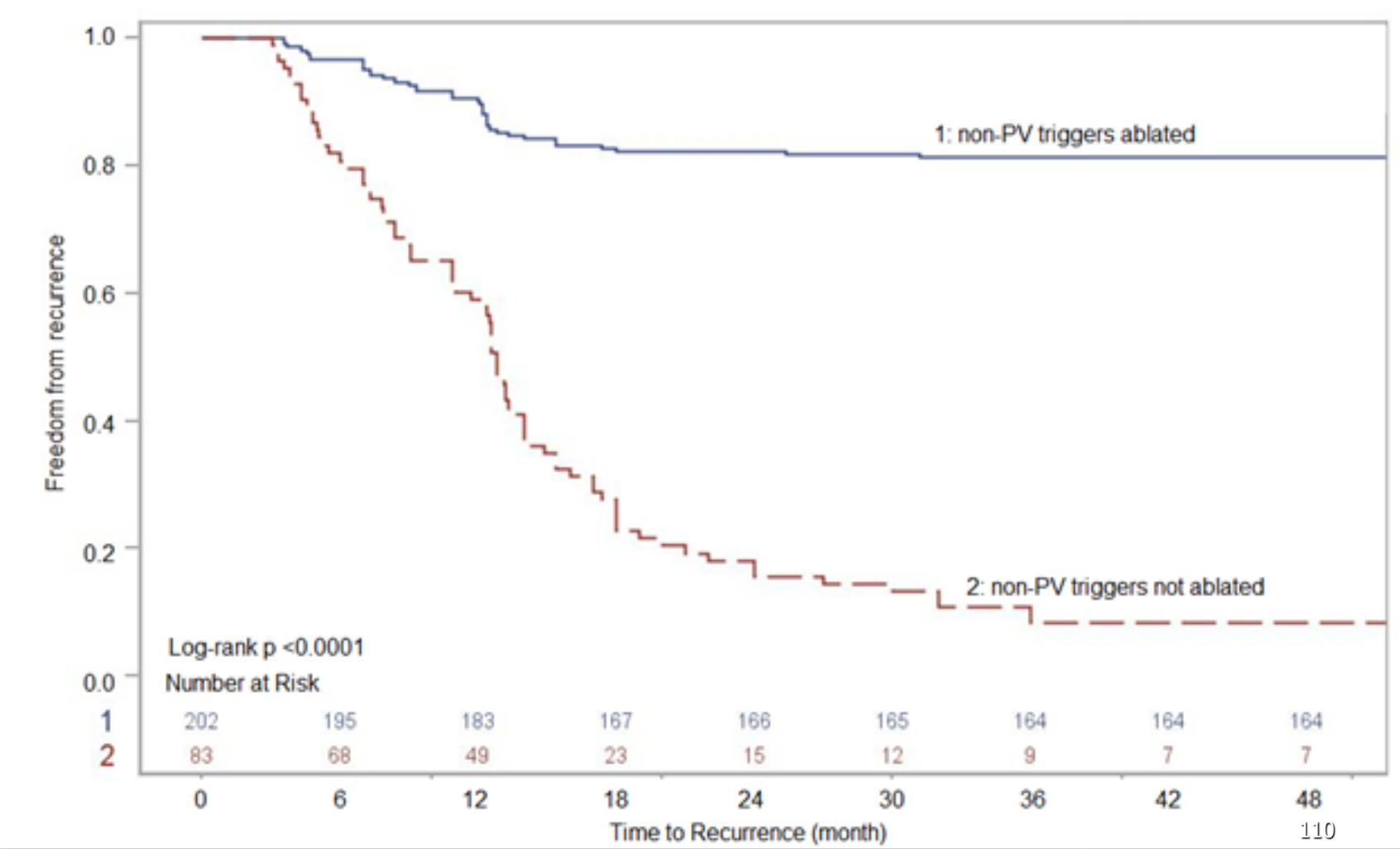
Incidence of PV Reconnection:



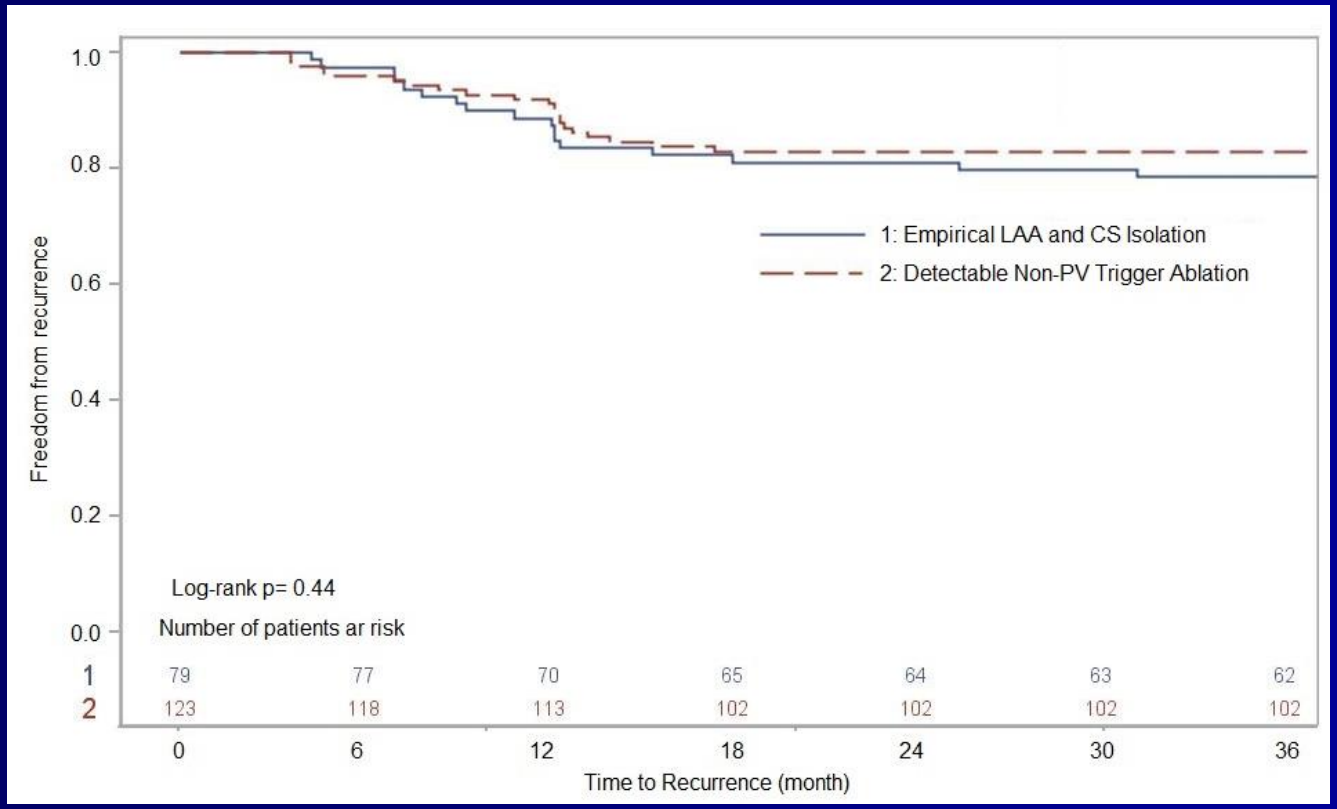
Index Procedure (n=305):

- PV reconnection: 226
- Non-PV triggers detected: 285
  - Non-PV Trigger Ablated=202:
    - PV reconnection: 123
    - Empirical LAA CS Isolation: 79
  - Non-PV Triggers Not Ablated=83:
    - All had PV reconnection
    - Infrequent PACs

KM Curve Showing Recurrence-free Survival after the Index Procedure



KM curve showing freedom from recurrence (off-AAD) in patients undergoing Empirical LAA and CS Isolation and Ablation of Detectable Non-PV at the index procedure.



Kaplan-Meier curve showing freedom from recurrence (off-AAD) in patients undergoing Empirical LAA and CS Isolation (n=79) and Ablation of Detectable Non-PV (n=123) at the index procedure. Sixty-two of 79 (78%) and 102 of 123 (83%) were successful off-AAD respectively.

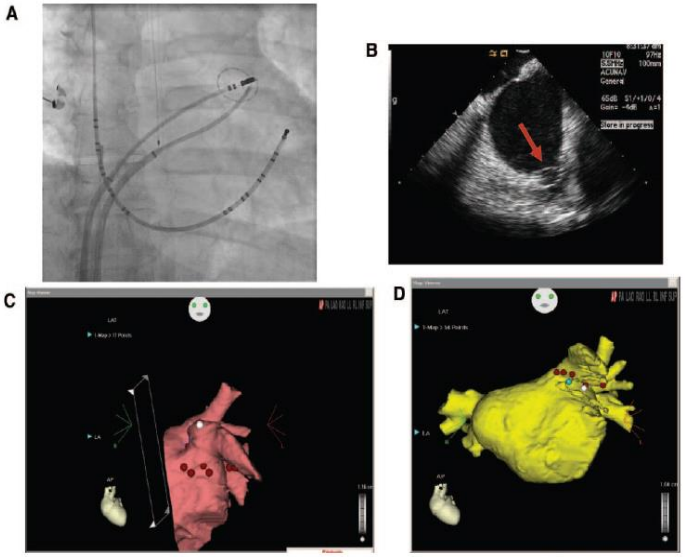
Outcomes In Long Standing Persistent Patients

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association®

Left Atrial Appendage : An Underrecognized Trigger Site of Atrial Fibrillation

Luigi Di Biase, J. David Burkhardt, Prasant Mohanty, Javier Sanchez, Sanghamitra Mohanty, Rodney Horton, G. Joseph Gallinghouse, Shane M. Bailey, Jason D. Zagrodzky, Pasquale Santangeli, Steven Hao, Richard Hongo, Salwa Beheiry, Sakis Themistoclakis, Aldo Bonso, Antonio Rossillo, Andrea Corrado, Antonio Raviele, Amin Al-Ahmad, Paul Wang, Jennifer E. Cummings, Robert A. Schweikert, Gemma Pelargonio, Antonio Dello Russo, Michela Casella, Pietro Santarelli, William R. Lewis and Andrea Natale



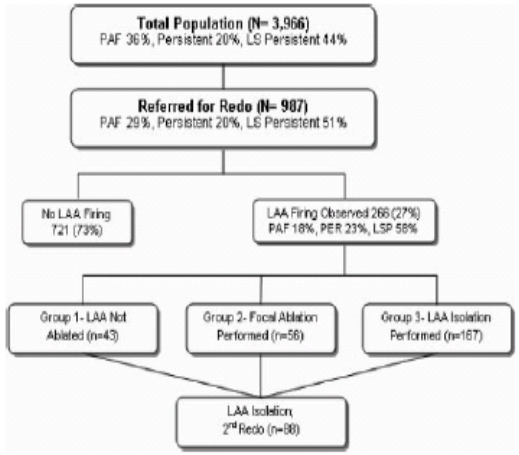
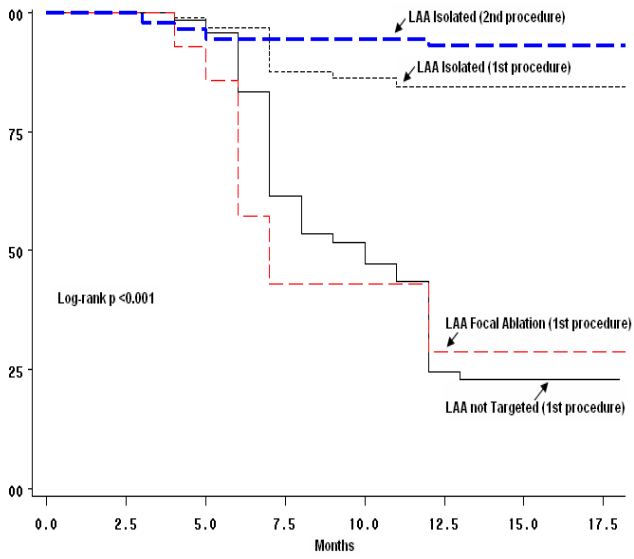


Figure 1. Flow chart showing the study design. PAF indicates paroxysmal AF; PER, persistent AF; and LSP, long-standing persistent AF.



Di Biase, Natale A, et al. Circulation. 2010;122:109-118.

Effect of Empirical Left Atrial Appendage Isolation on Long-term Procedure Outcome in Patients with Long-standing Persistent AF undergoing Ablation: Results from the *BELIEF* Randomized Trial

ClinicalTrials.gov Identifier: NCT01362738

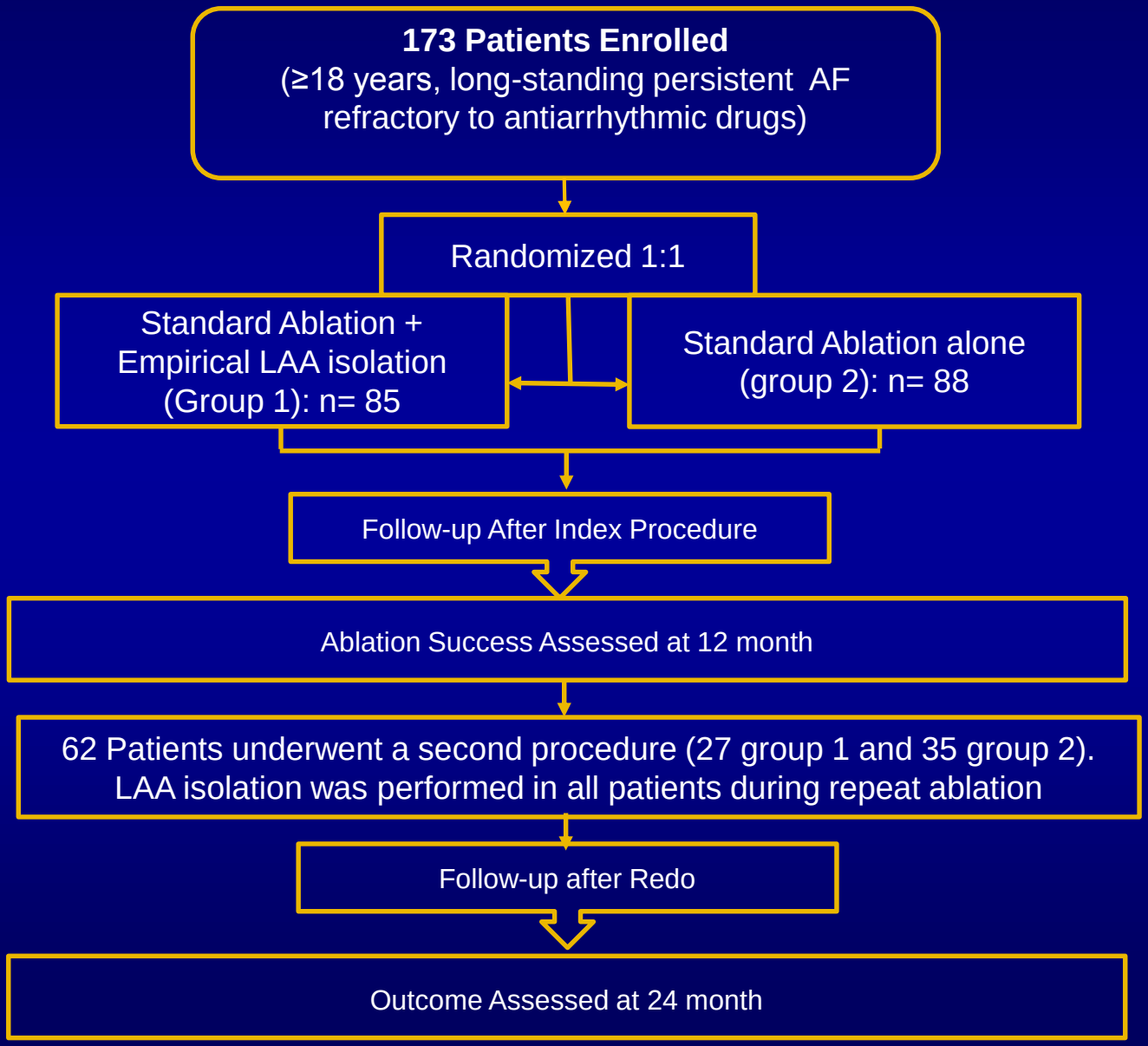
Luigi Di Biase, J. David Burkhardt, MD, Prasant Mohanty, Sanghamitra Mohanty, , Javier E. Sanchez, Chintan Trivedi, Mahmut Güneş, Yalçın Gökoğlan, Carola Gianni, Rodney P. Horton, G. Joseph Gallinghouse, Shane Bailey, Jason D. Zagrodzky, Steven C. Hao, Richard H. Hongo, Salwa Beheiry, Pasquale Santangeli, Michela Casella, Antonio Dello Russo, Amin Al-Ahmad, Patrick Hranitzky, Dhanujaya R. Lakkireddy, Claudio Tondo, **Andrea Natale.**

- Texas Cardiac Arrhythmia Institute at St. David's Medical Center, Austin, Texas, USA;
- California Pacific Medical Center, San Francisco, California, USA;
- University of Kansas, Kansas City, USA;
- Cardiac Arrhythmia Research Centre, Centro Cardiologico Monzino IRCCS, Milan, Italy;

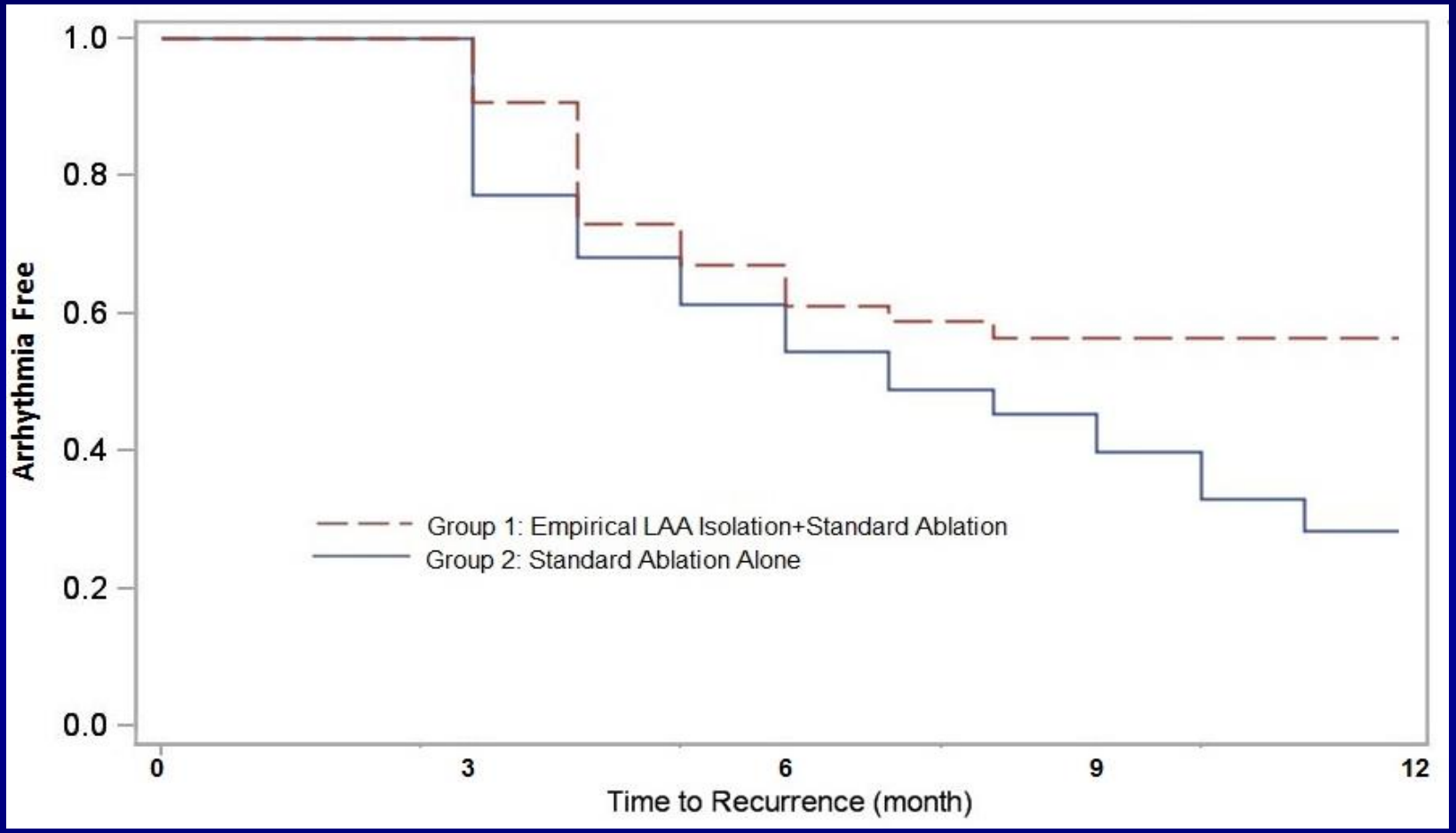
Di Biase, Natale et al JACC 2017

Di Biase, Natale et al ESC 2015

Study Design



Kaplan–Meier curves: single procedure success rate



At the 12 month follow-up, 48(56%) in group 1 and 25 (28%) in group 2 were recurrence-free off-AAD after a single procedure. (Log-rank p=0.001, unadjusted HR 1.92 [1.3 to 2.9]).

Di Biase, Natale et al JACC 2017

Long-Term Effect of Goal Directed Weight Management in an Atrial Fibrillation Cohort: A Long-term Follow-Up StudY

LEGACY AF

AF and BMI ≥ 27 kg/m^2

N = 355

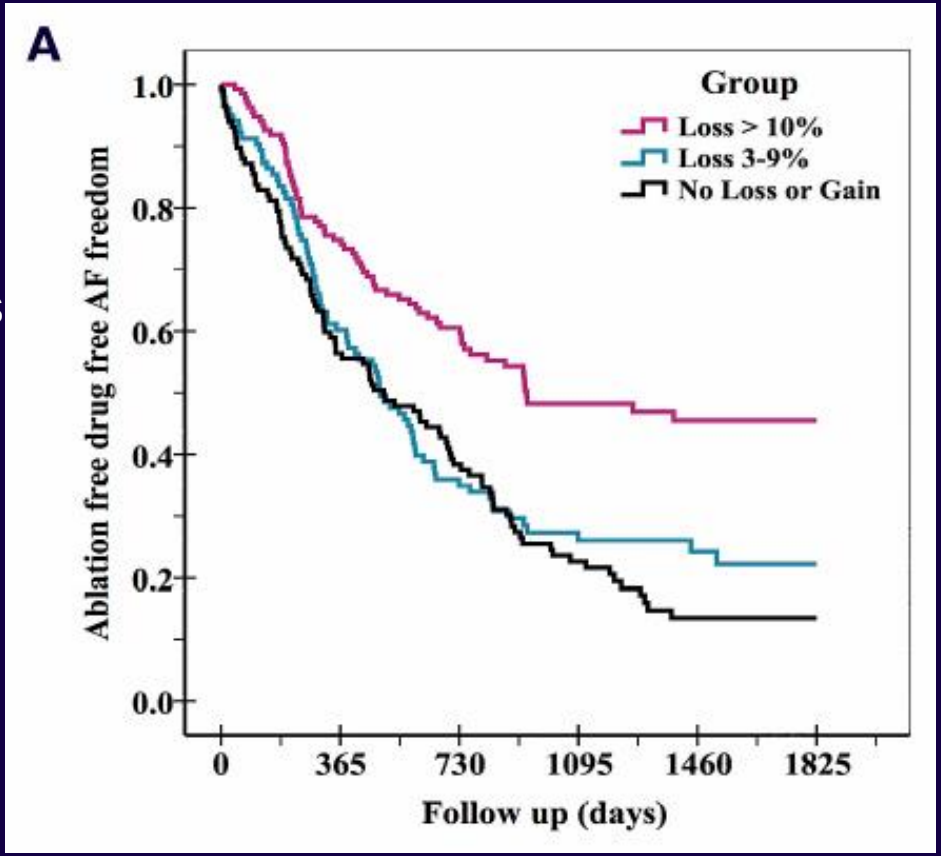
Weight loss

Observational study

Freedom from AF

FU = mean 47 months

We need…
RCTs



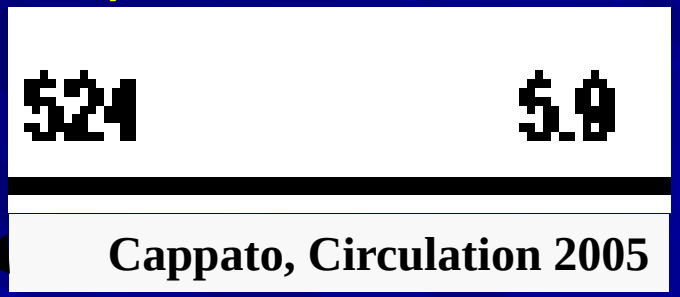
Pathak et al. J Am Coll Cardiol. 2015; epub ahead of print

Worldwide Survey on the Methods, Efficacy, and Safety of Catheter Ablation for Human Atrial Fibrillation

TABLE 4. Major Complications

Complication Type	No. of Patients	% of Patients
For all types of procedures (n=8745 patients)		
Periprocedural death	4	0.05
Tamponade	107	1.22
Sepsis, abscesses, or endocarditis	1	0.01
Pneumothorax	2	0.02
Hemothorax	14	0.16
Permanent diaphragmatic paralysis	10	0.11
Femoral pseudoaneurysm	47	0.53
Arteriovenous fistulae	37	0.42
Valve damage	1	0.01
Aortic dissection	3	0.03
For procedures involving left atrial ablation (n=7154 patients)		
Stroke	20	0.28
Transient ischemic attack	47	0.66
PV stenosis		
No. with >50% stenosis		
Acute	23	0.32
Chronic	94	1.31
No. with closure		
Acute	2	0.03
Chronic	15	0.21
Patients with symptoms		
Acute	3	0.04
Chronic	41	0.57
Patients undergoing intervention		
Percutaneous	51	0.71
Surgical	2	0.03
Grand total	524	5.9

With drugs, the overall discontinuation rate due to adverse events range from 11 to 18% (mortality ranged from 4 to 7%).



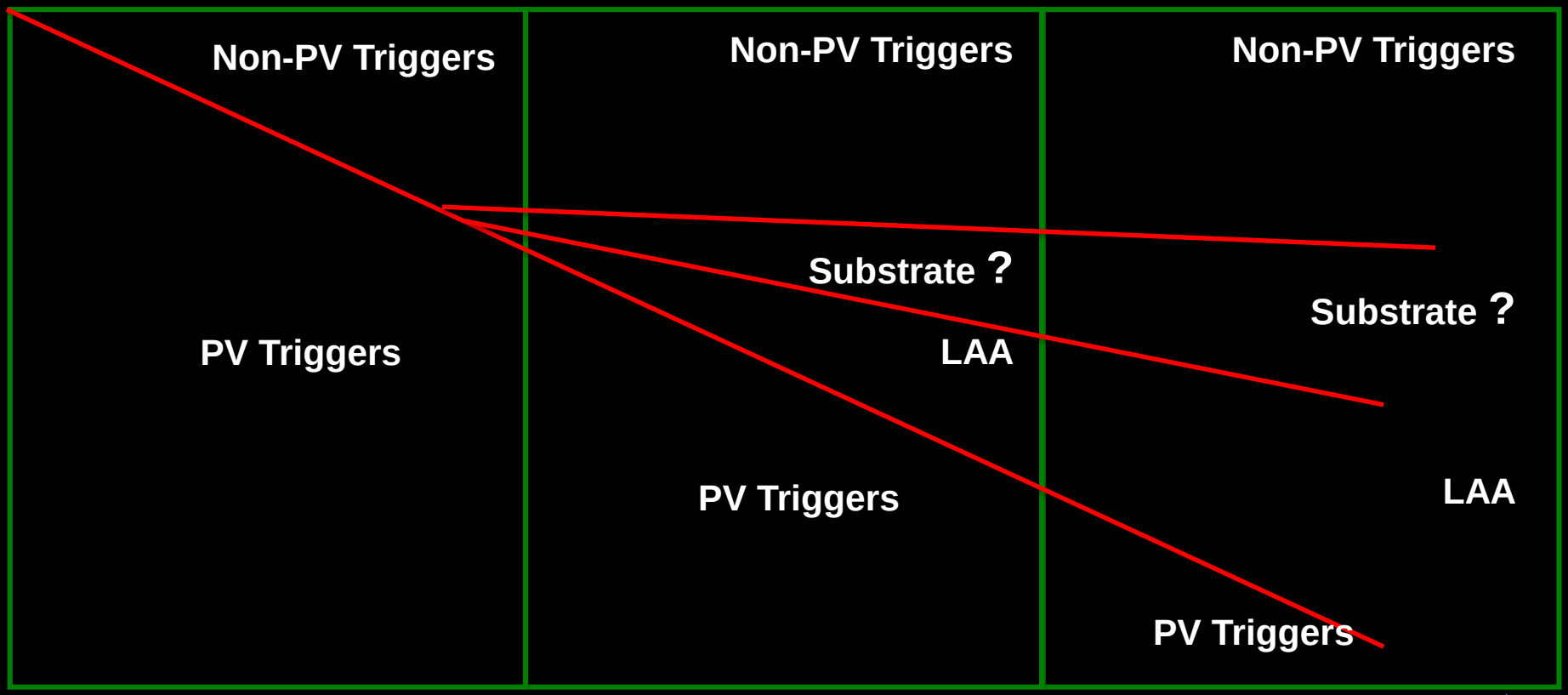
Cappato, Circulation 2005

Complication rate: 3,9%

Deaths: 0,1%

Cappato, 2008

Relative contribution of different ablation targets in the AF disease continuum



“I have tremor cordis on me: my heart dances;

but not for joy; not joy”

The Winter’s Tale, 1610, William Shakespeare

ATRIAL FIBRILLATION

AF management: Final Considerations

- Based on the present evidences, in patients who have failed one drug, ablation could be the next therapeutic step (class I, level of evidence A)
- In selected patients ablation could be consider as first line therapy (class IIa, level of evidence B)

Conclusion of the CABANA Trial

- Ablation did not produce a significant reduction in the primary endpoint and all-cause mortality.
- The results were affected by cross-overs in both directions and lower than expected event rates.
- Ablation significantly reduced mortality or CV hospitalization by 17% compared to drug therapy.
- There also was a significant 47% reduction in recurrent AF with ablation compared to drug therapy.
- A 33% reduction in the primary endpoint and 40% mortality risk reduction was present when patients actually *underwent* ablation *(treatment received).*
- Ablation is an acceptable treatment strategy for treating AF with low adverse event rates even in higher risk patients.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