AF ABLATION AFTER THE STAR-AF TRIAL

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A Case- A 70 y.o. man with a few months h/o of fatigue, decreased effort tolerance

- h/o hypertension- Rx: Bisoprolol 5 mg
- Echo- LVEF 55%
- LA mildly enlarged
- 24hr holter- AF 90 (60 -140)
- Started on a NOAC, Flecainide
- DC CVN > NSR
- AF recurrence- 2 months. What now?

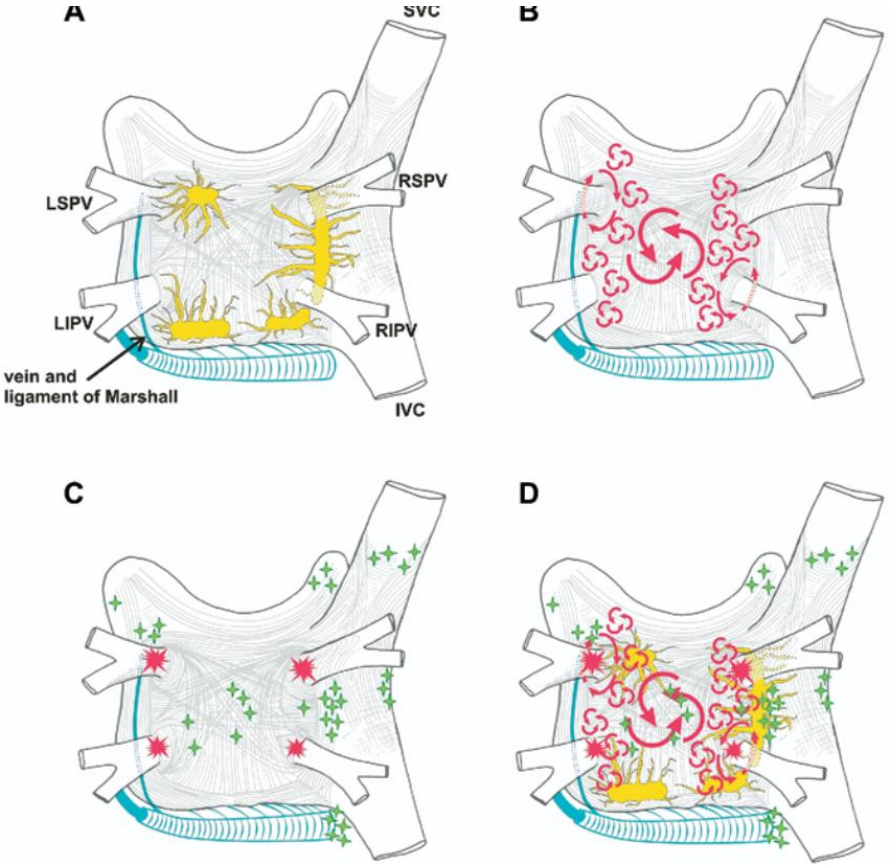
A 70 y.o. with recurrent persistent AF

What will you do?

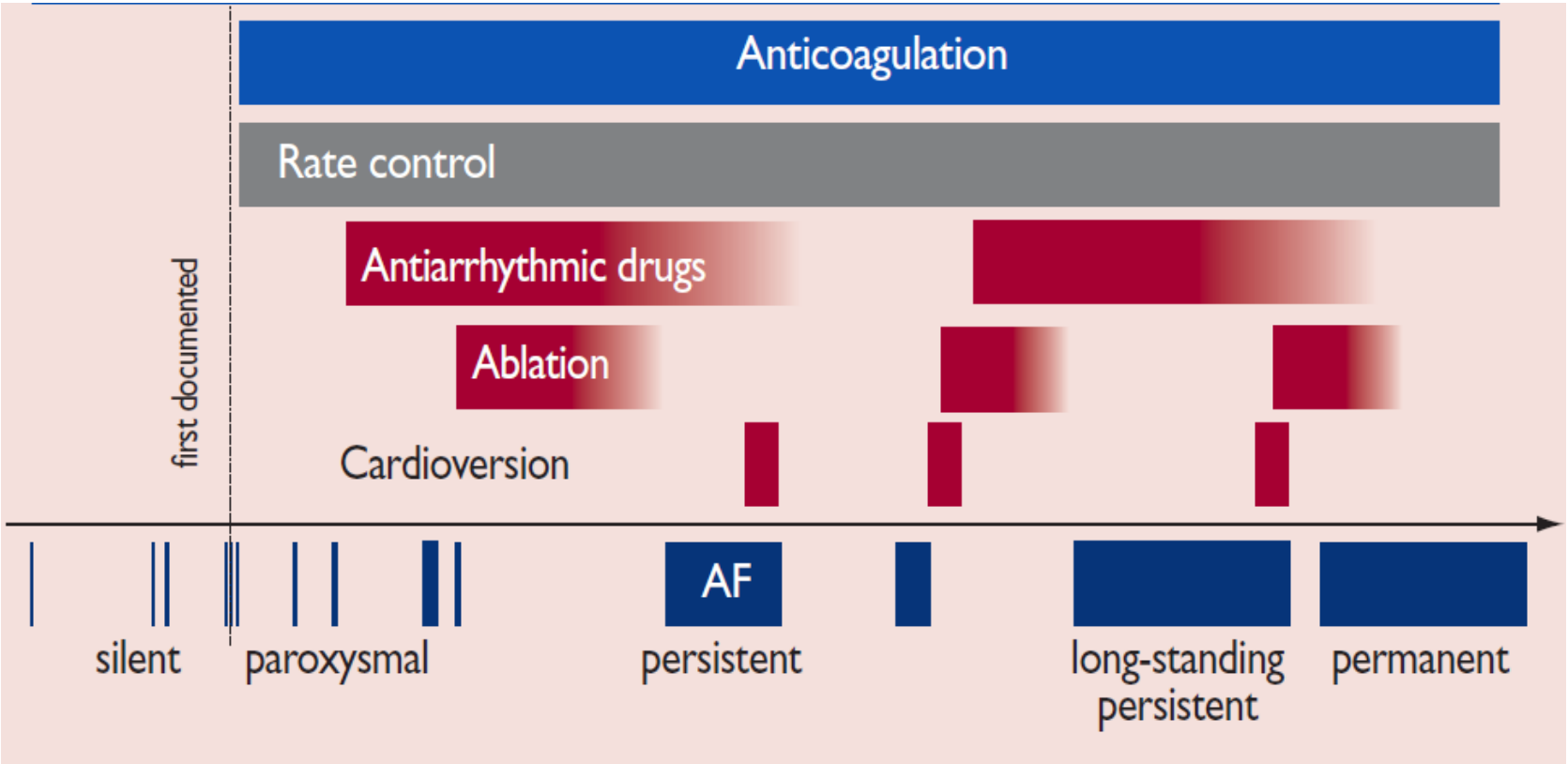
1. Send for a repeat CVN
2. Change the anti-arrhythmic drug (+/- repeat CVN)
3. Send for PVI
4. Stop Flecainide and follow up only

Pathophysiology: A complex interaction between triggers and tissue.

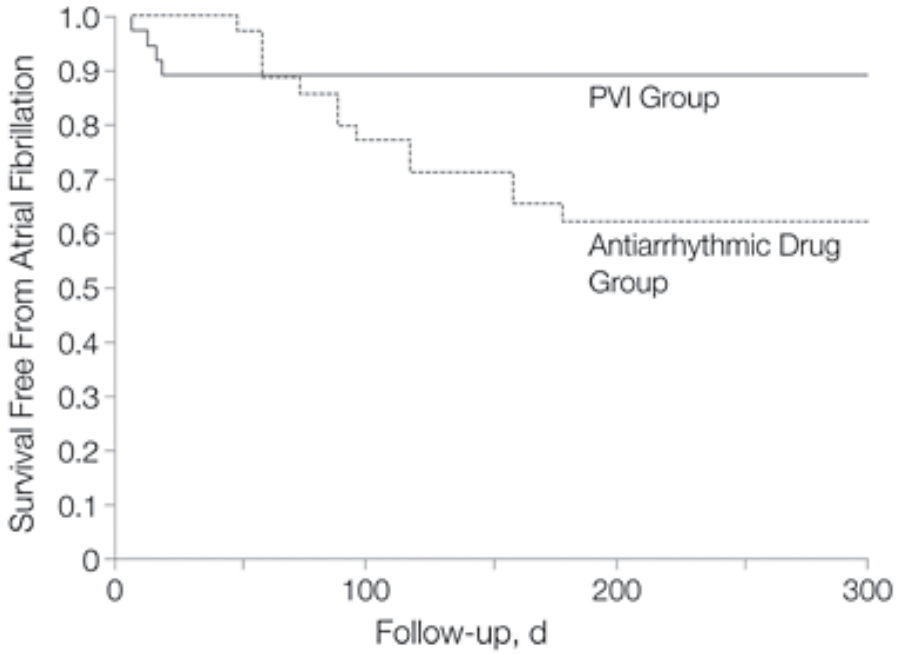
- Current mechanisms to sustain AF:
  - A single focus firing at a short CL
  - A single, stable re-entrant circuit of short CL
  - Multiple, unstable re-entrant circuits of short CL



Natural History of AF



PVI Better than Drugs

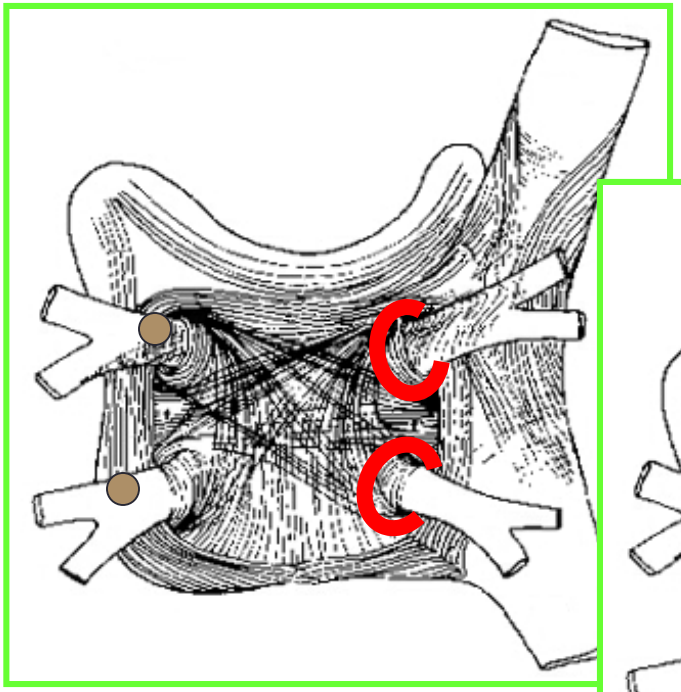


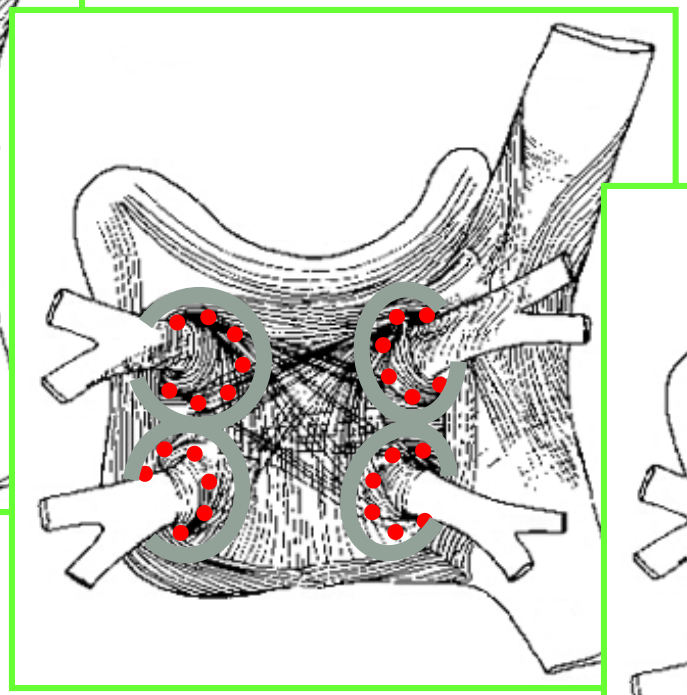
No. at Risk							
PVI Group	32	28	28	28	28	28	28
Antiarrhythmic Drug Group	35	34	23	19	13	13	13

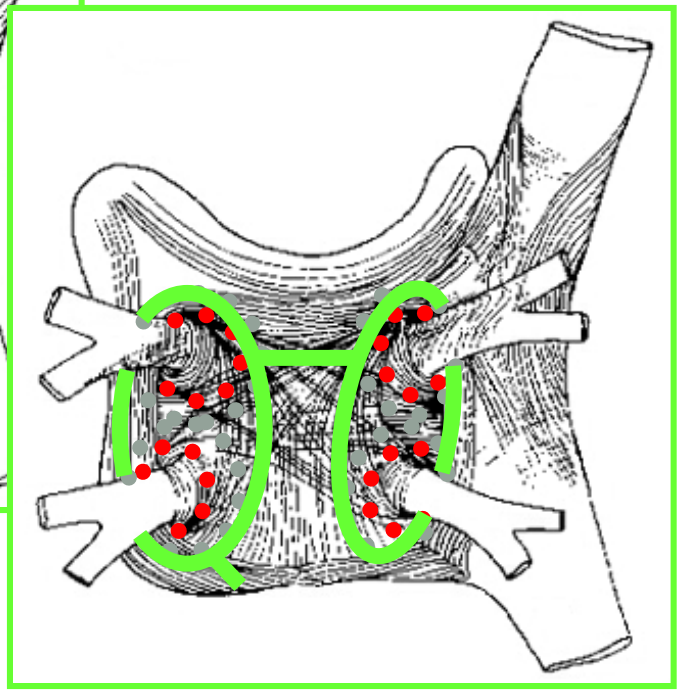
Natale A, et al. JAMA 2005

Catheter Ablation

Pulmonary Vein Isolation







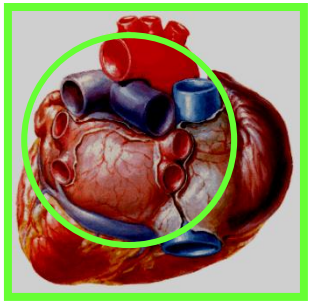
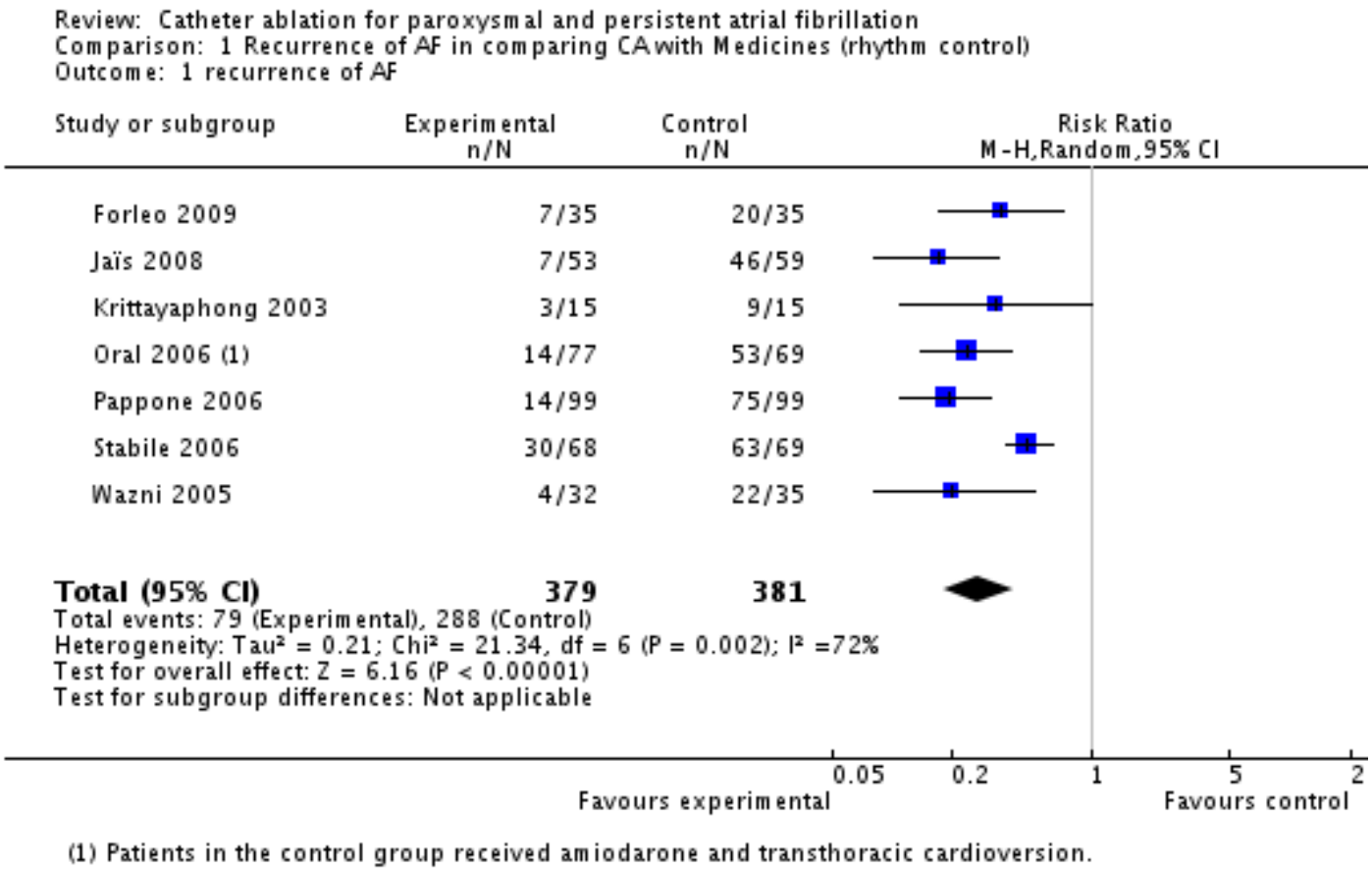


Table 18 Randomized clinical trials of catheter ablation vs. antiarrhythmic drugs or no treatment in AF

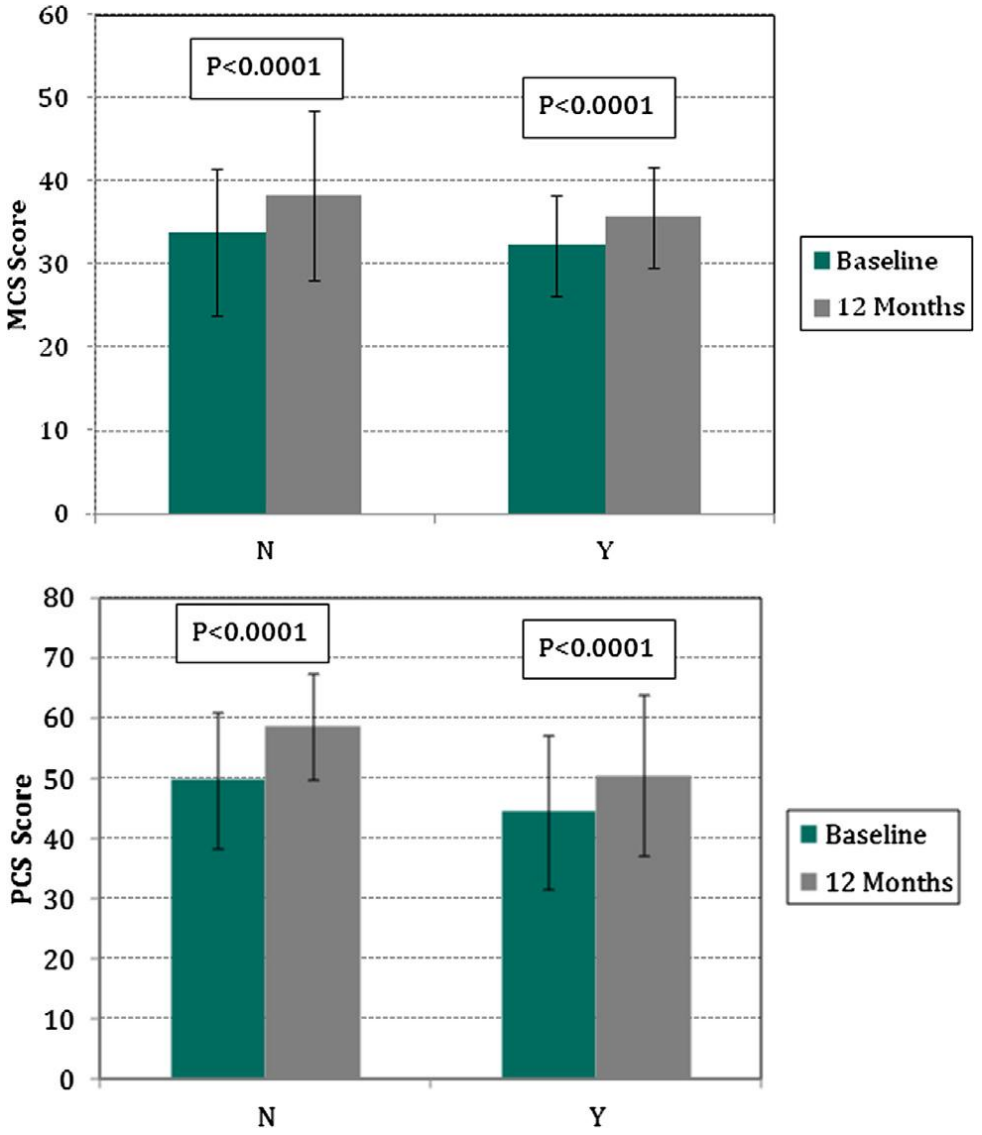
Study	Reference	Patients (n)	Age, years	Type of AF	Previous use of AAD	Ablation technique	Repeat ablation in the ablation group	Crossed to ablation in the AAD group	AF free at 1 year	
									Ablation	AAD
Krittayaphong *et al.* 2003	Online	30	55 ± 10 (ablation) 47 ± 15 (AAD)	Paroxysmal, persistent	≥1[a]	PVI + LA lines + CTI ablation + RA lines	Not stated	Not stated	79%	40%
Wazni *et al.* 2005 (RAAFT)	134	70	53 ± 6 (ablation) 54 ± 8 (AAD)	Mainly paroxysmal	No	PVI	12%[b]	49%[c]	87%	37%
Stabile *et al.* 2005 (CACAF)[d]	Online	245	62 ± 9 (ablation) 62 ± 10 (AAD)	Paroxysmal, persistent	≥2	PVI + LA lines ± CTI ablation	No exact data	57%	56%	9%
Oral *et al.* 2006[e]	Online	245	57 ± 9	Persistent	≥1 (mean 2.1 ± 1.2)	CPVA	26% for AF; 6% for LA flutter	77%	74%	4%
Pappone *et al.* 2006 (APAF)	135	198	55 ± 10 (ablation) 57 ± 10 (AAD)	Paroxysmal	≥2 (mean 2 ± 1)	CPVA + CTI ablation	6% for AF; 3% for atrial tachycardia	42%	86%	22%
Jais *et al.* 2008 (A4 study)	133	112	51 ± 11	Paroxysmal	≥1	PVI ± LA lines ± CTI ablation	Mean 1.8 ± 0.8, median 2 per patient	63%	89%	23%
Forleo *et al.* 2008[f]	Online	70	63 ± 9 (ablation) 65 ± (AAD)	Paroxysmal, persistent	≥1	PVI ± LA lines ± CTI ablation	Not stated	Not stated	80%	43%
Wilber *et al.* 2010 (Thermocool)[g]	96	167	55.5 (ablation) 56.1 (AAD)	Paroxysmal	≥1 (mean 1.3)[h]	PVI ± LA lines ± CFAEs ± CTI ablation ± RA lines	12.6% within 80 days after 1st procedure[i]	59%[c]	66%	16%
Packer *et al.* 2010 (STOP-AF)[j]	Online	245	56.7 (ablation) 56.4 (AAD)	Paroxysmal	≥1[b]	Cryo-PVI ± LA lines	19% within 90 days after 1st procedure	79%	69.9%	7.3%

Meta-Analysis of PVI vs. AADs



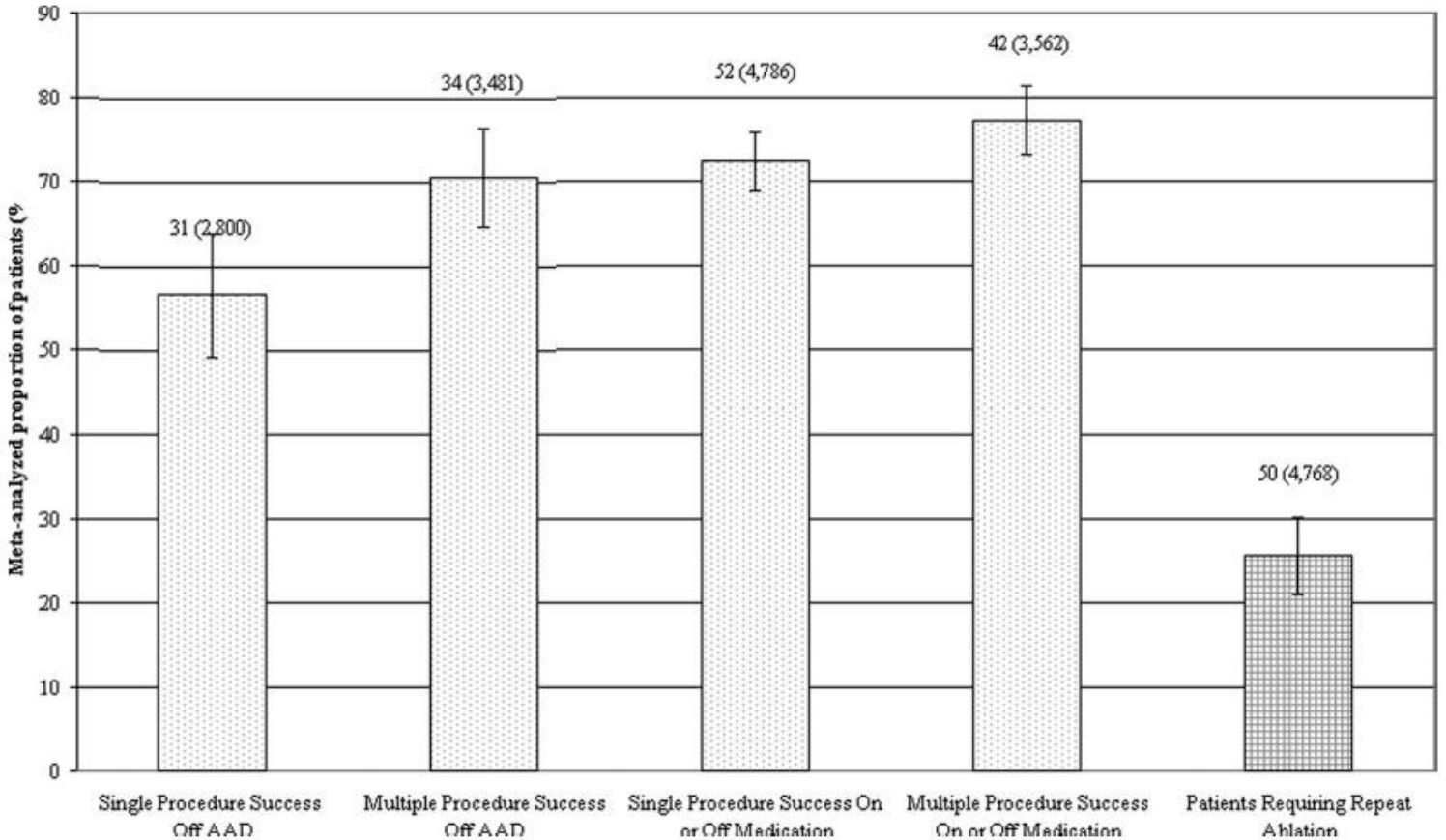
Chen HS, Cochrane Database Syst Rev. 2012

Ablation Improves QOL



Mantovan R, Can J Cardiol 2013

Meta-Analysis of PVI Efficacy



Culkins H, et al, Circ Arrhythm Electrophysiol , 2009

PVI Long Term Success

- 36% persistent AF
- Single Procedure

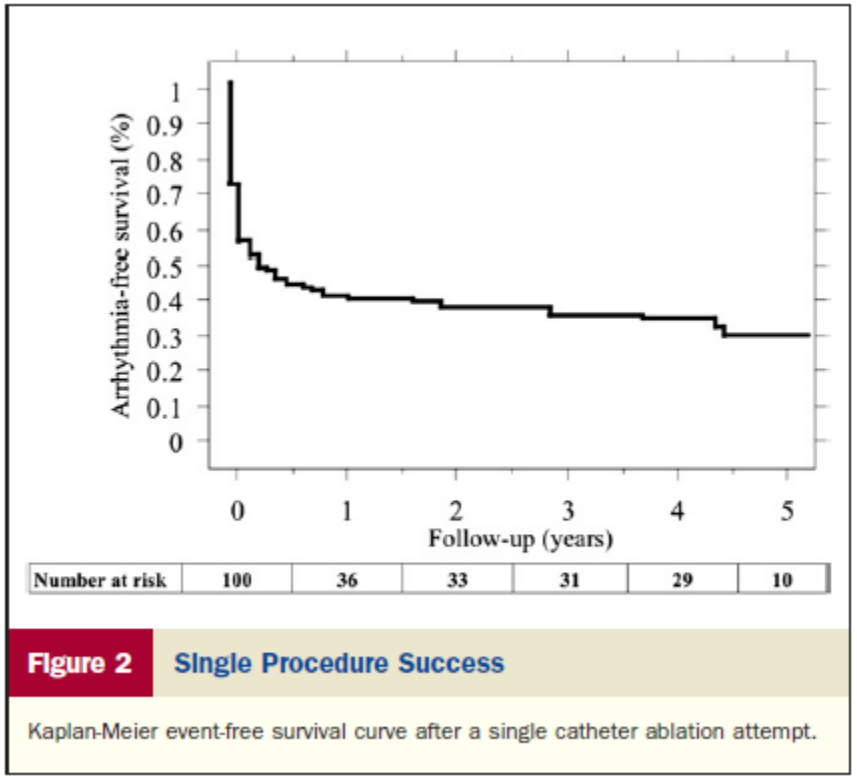
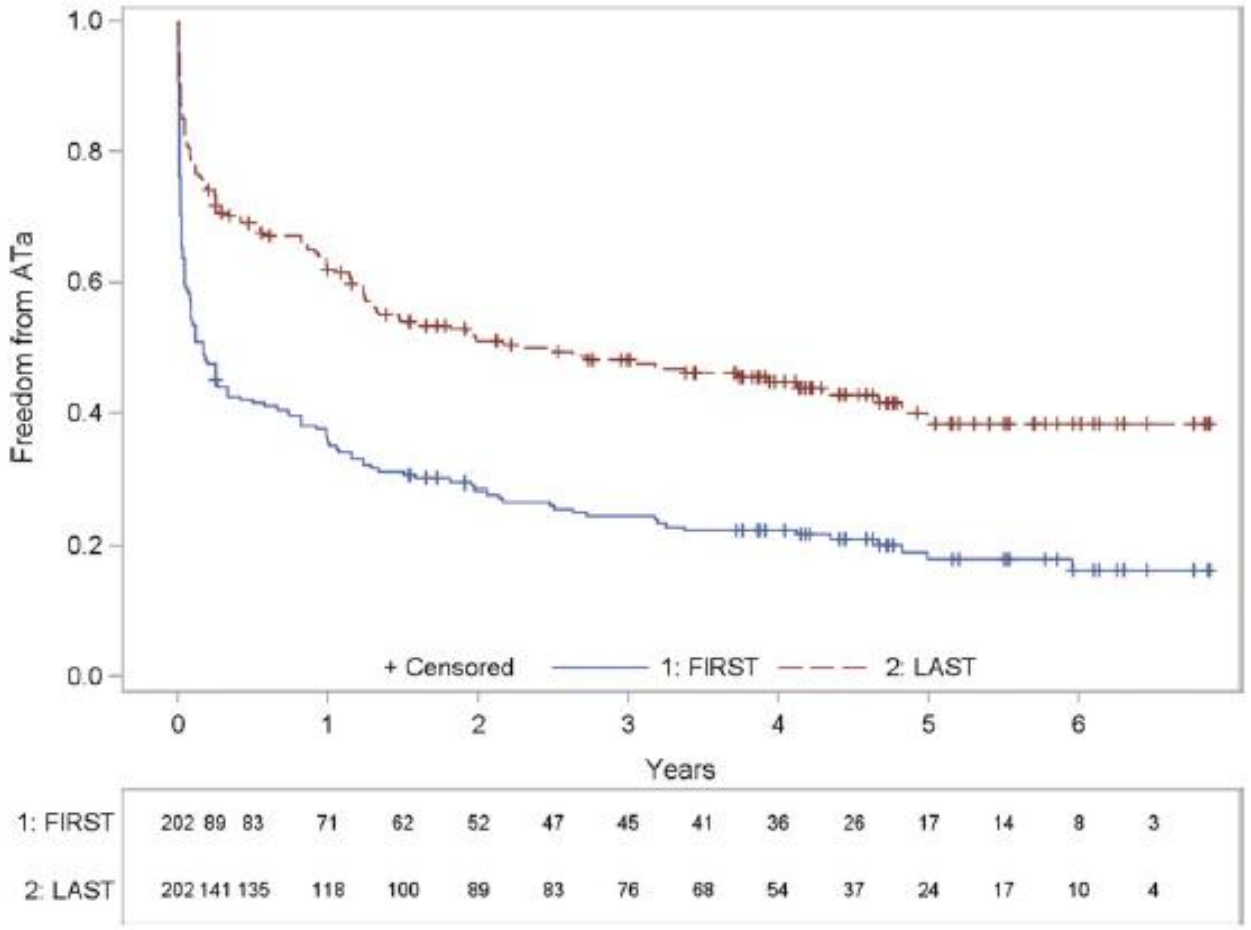


Figure 2 **Single Procedure Success**

Kaplan-Meier event-free survival curve after a single catheter ablation attempt.

Weerasooriya R …, Jais P. JACC 2011

PVI for Persistent AF



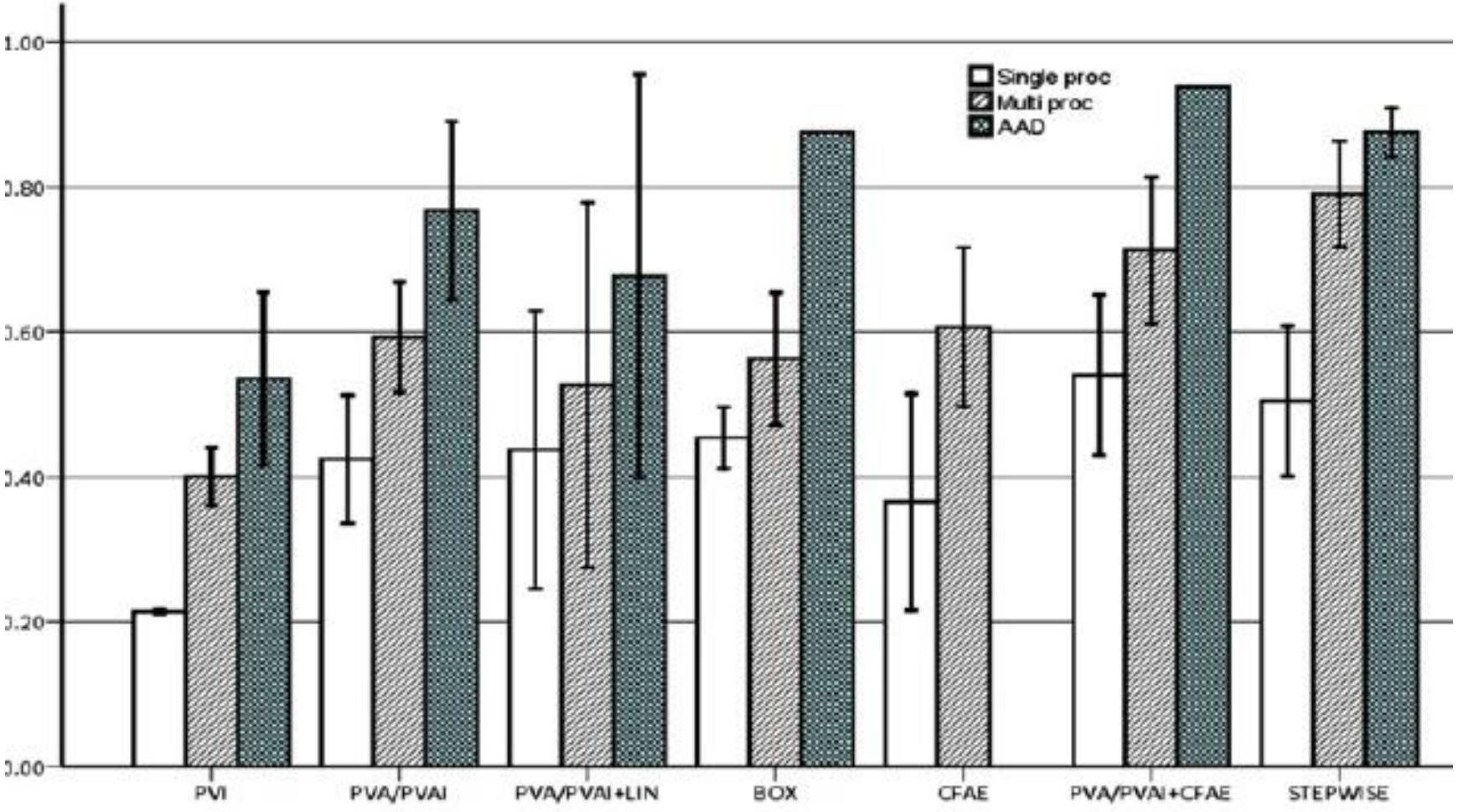
Tilts RR, et al. JACC 2012

Back to the case- decided on PVI. Patient arrives in AF

- All vein are isolated- patient is still in AF.
- What will be your next step?

1. Identify and ablate complex atrial electrograms (CFAEs) until AF converts into NSR
2. Perform a roof line and/ or mitral isthmus line
3. Ablate and Isolate the SVC
4. Shock the patient into NSR

Clinical Success of Various Techniques in Pers. AF



Brooks AG et al, Heart Rhythm 2010

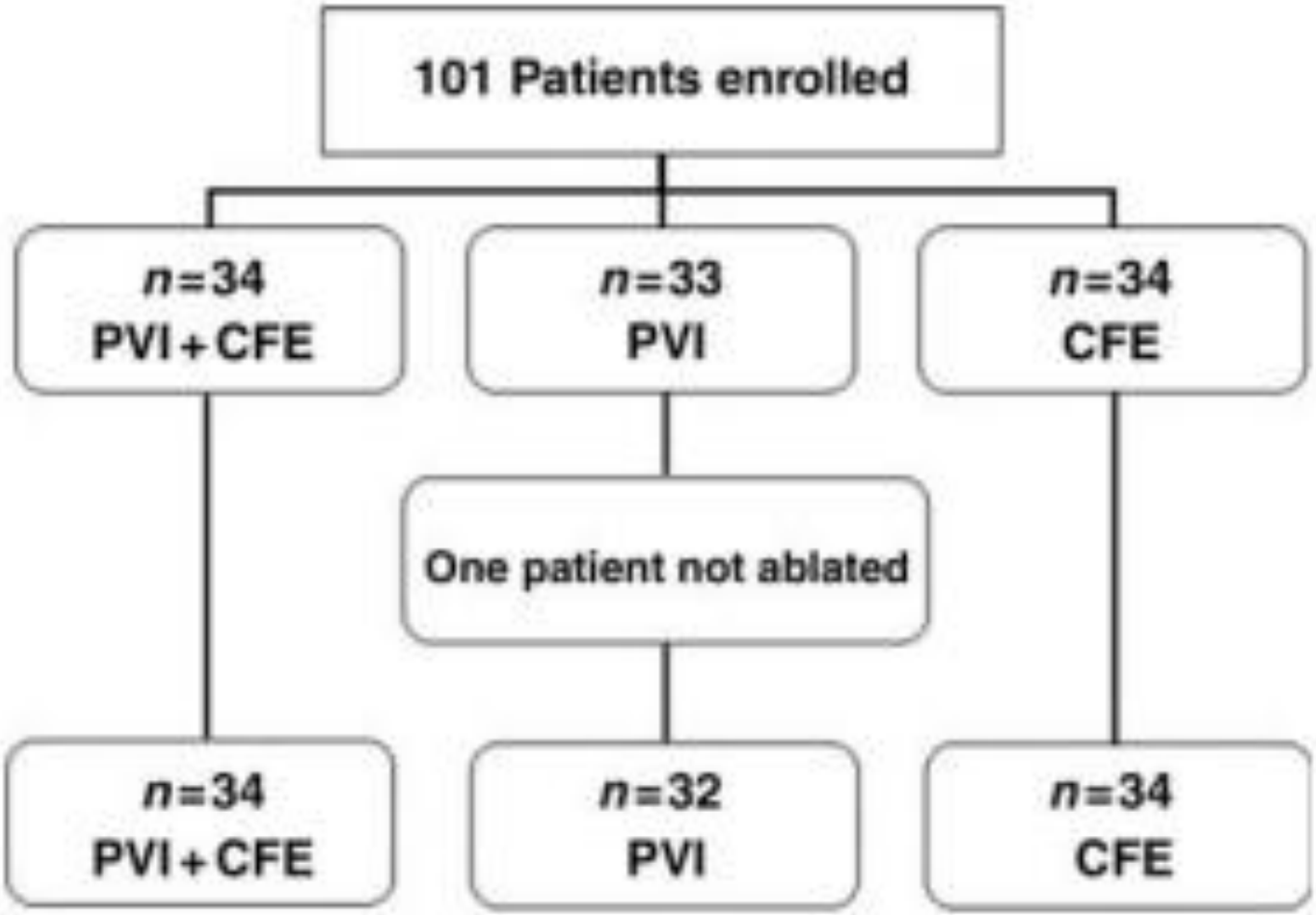
Different Strategies for Persistent AF

	Group 1 CPVA n = 47	Group 2 PVAI n = 48	Group 3 CFAE + PVAI n = 49	*P* value
Mean follow-up (mo)				
Patients free of AF/AT after a single procedure (primary endpoint)	5 (11%)	19 (40%)	30 (61%)	<.001
Patients free of AF/AT after 2 procedures and no AADs (secondary endpoint)	8 (17%)	27 (56%)	39 (80%)	<.001
Patients free of AF/AT after 1 or 2 procedures and AADs (secondary endpoint)	13 (28%)	41 (83%)	46 (94%)	<.001

Elayi CS et al, Heart Rhythm 2008

Substrate and Trigger Ablation for Reduction of Atrial Fibrillation (STAR AF)

- First Ablation
- Failed ≥ 1 AAD
- 1/3 persistent

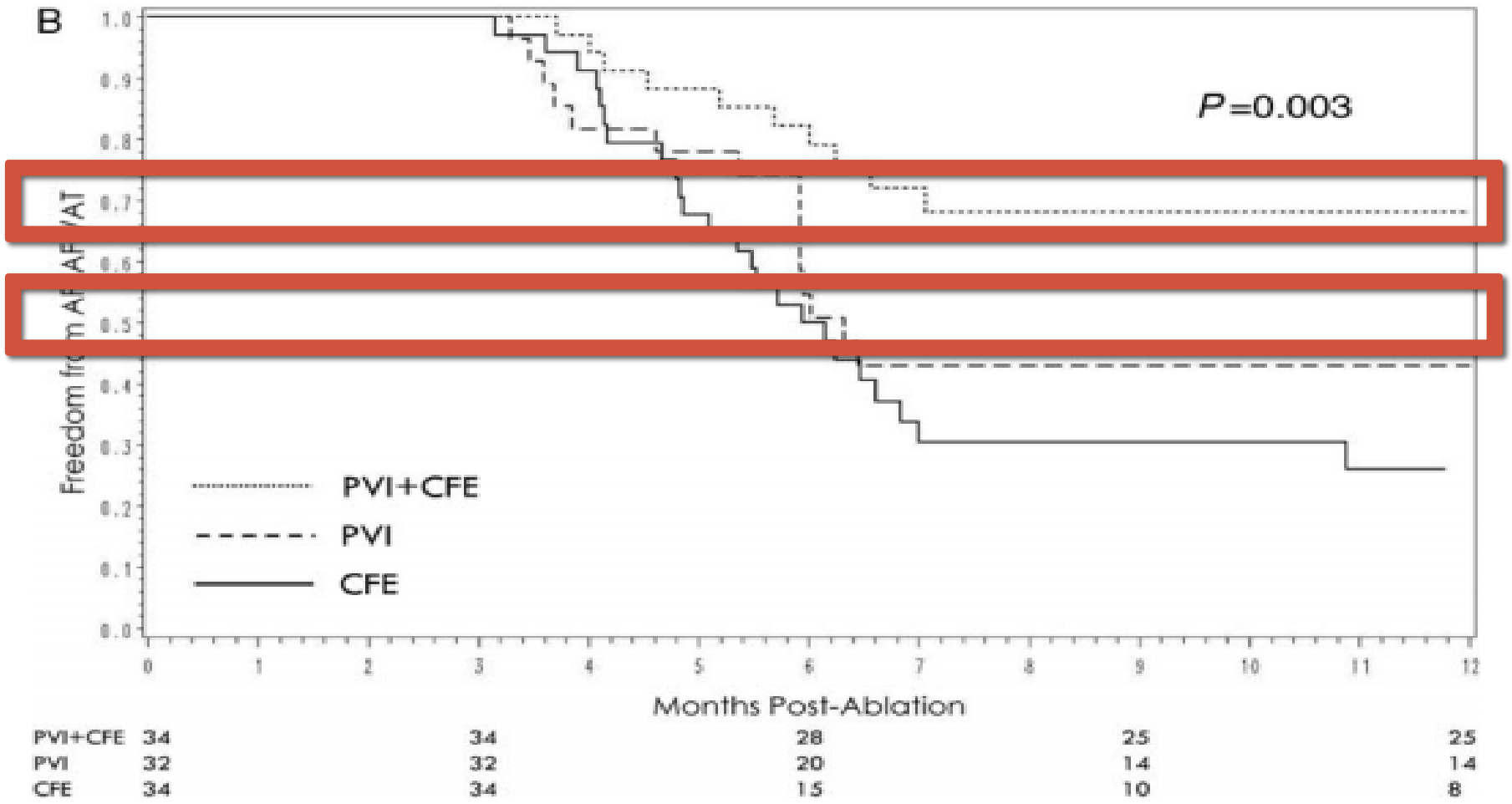


Verma A et al, Eur Heart J 2010

CFAE

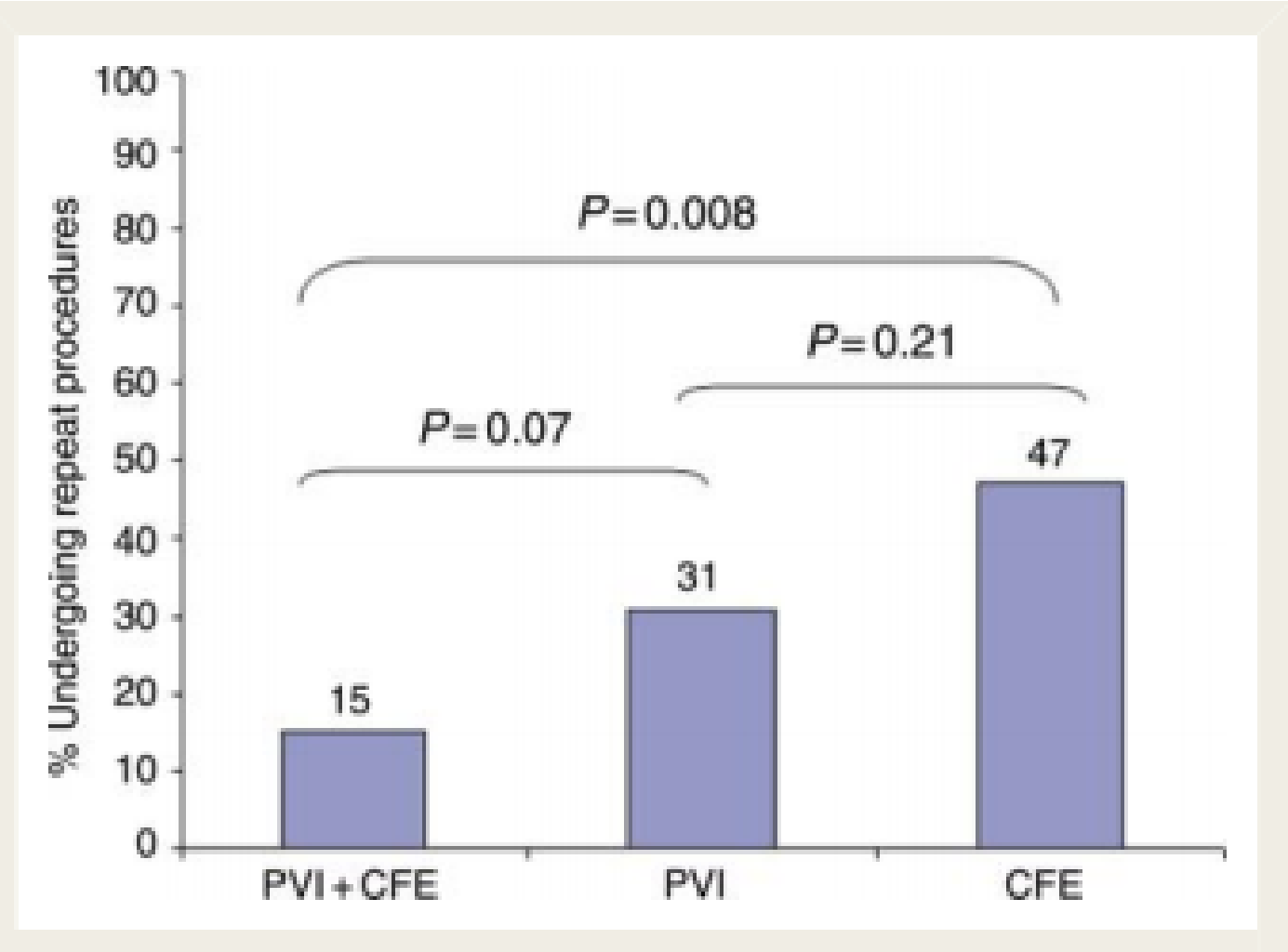
Peak-to-peak sensitivity (minimum detection threshold, avoids detecting noise)	0.03–0.05 mV
EGM refractory period (avoids double-counting a single EGM with multiple components)	35–45 ms
EGM width (avoids detection of broader, far-field EGMs)	15–20 ms
EGM segment length (total recording duration at each point, obtains a mean CL for that point)	5 s
Interpolation (maximum distance between points which will be used to assign average values for a vertex)	4–6 mm
Internal/external projection (avoids collection of EGMs from electrodes that are not in good contact with map shell)	4–6 mm

Substrate and Trigger Ablation for Reduction of Atrial Fibrillation (STAR AF)



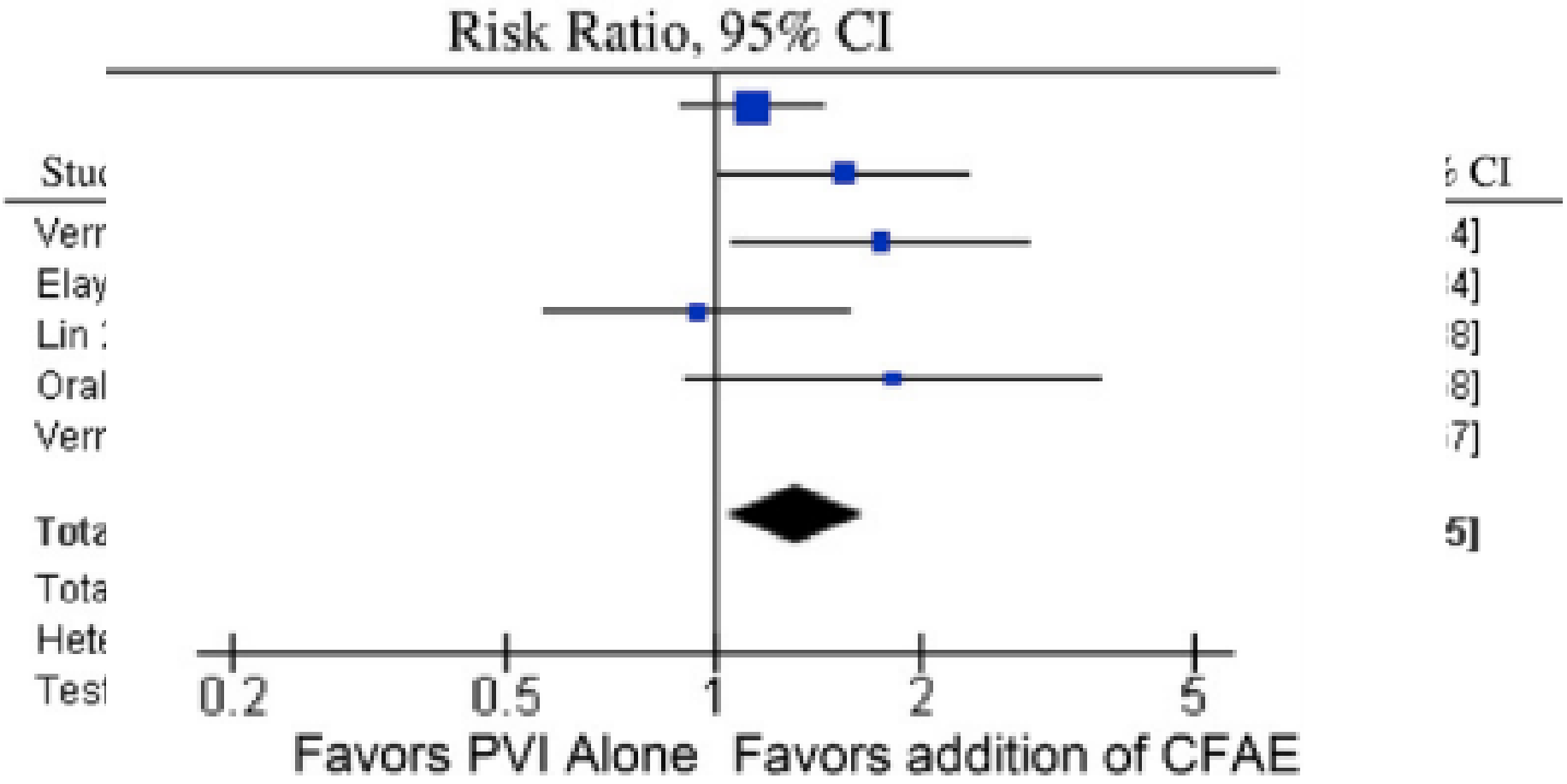
Verma A et al, Eur Heart J 2010

Substrate and Trigger Ablation for Reduction of Atrial Fibrillation (STAR AF)



Verma A et al, Eur Heart J 2010

PVI/CFEA in Pers. AF Meta-Analysis



Hayward RM et al, Heart Rhythm 2011

STAR-AF II

- To compare the efficacy of three different AF ablation strategies in patients with persistent AF:

  (1) Pulmonary vein isolation (PVI) alone

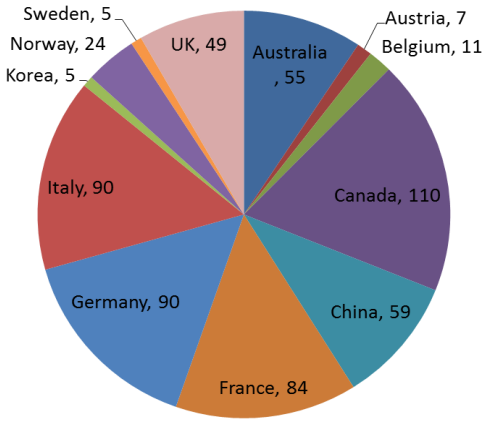
  (2) PVI plus complex fractionated electrograms (PVI+CFE)

  (3) PVI plus linear ablation (PVI+Lines).

Verma A et al, ESC 2014

STAR-AF II: Methods - Patients

- 589 patients were recruited from 48 experienced ablation centers in 12 countries
- Inclusion: symptomatic persistent AF (a sustained episode > 7 days and < 3 years) refractory to at least one antiarrhythmic drug undergoing first-time ablation
- Exclusion: paroxysmal AF, sustained AF episode > 3 years, left atrial diameter > 60 mm



Verma A et al, ESC 2014

STAR-AF II: Methods – Ablation Strategy

- Patients were randomized 1:4:4 to the three strategies:
  - PVI, PVI+CFE, PVI+Lines
- PVI = PV antral isolation with endpoint of entrance and exit block by a circular mapping catheter
- PVI+CFE = PVI followed by mapping and ablation of complex fractionated electrograms during AF identified by validated software in the 3D mapping system (Ensite Velocity)
- PVI+Lines = PVI followed by a *left atrial roof line* and *a line along the mitral valve isthmus* with endpoint of bidirectional block confirmed by pre-specified pacing maneuvers

Verma A et al, ESC 2014

STAR-AF II: Results

- 79% of patients presented to EP lab in spontaneous AF
- Successful PV isolation obtained in 97% of all patients (all groups)
- CFEs were eliminated in 80% of patients
  - 11% not ablated because AF non-inducible after PVI
  - 9% all CFE could not be eliminated
- Both lines with block achieved in 74% of patients
  - Roof line only 93%
  - Mitral line only 75%

Verma A et al, ESC 2014

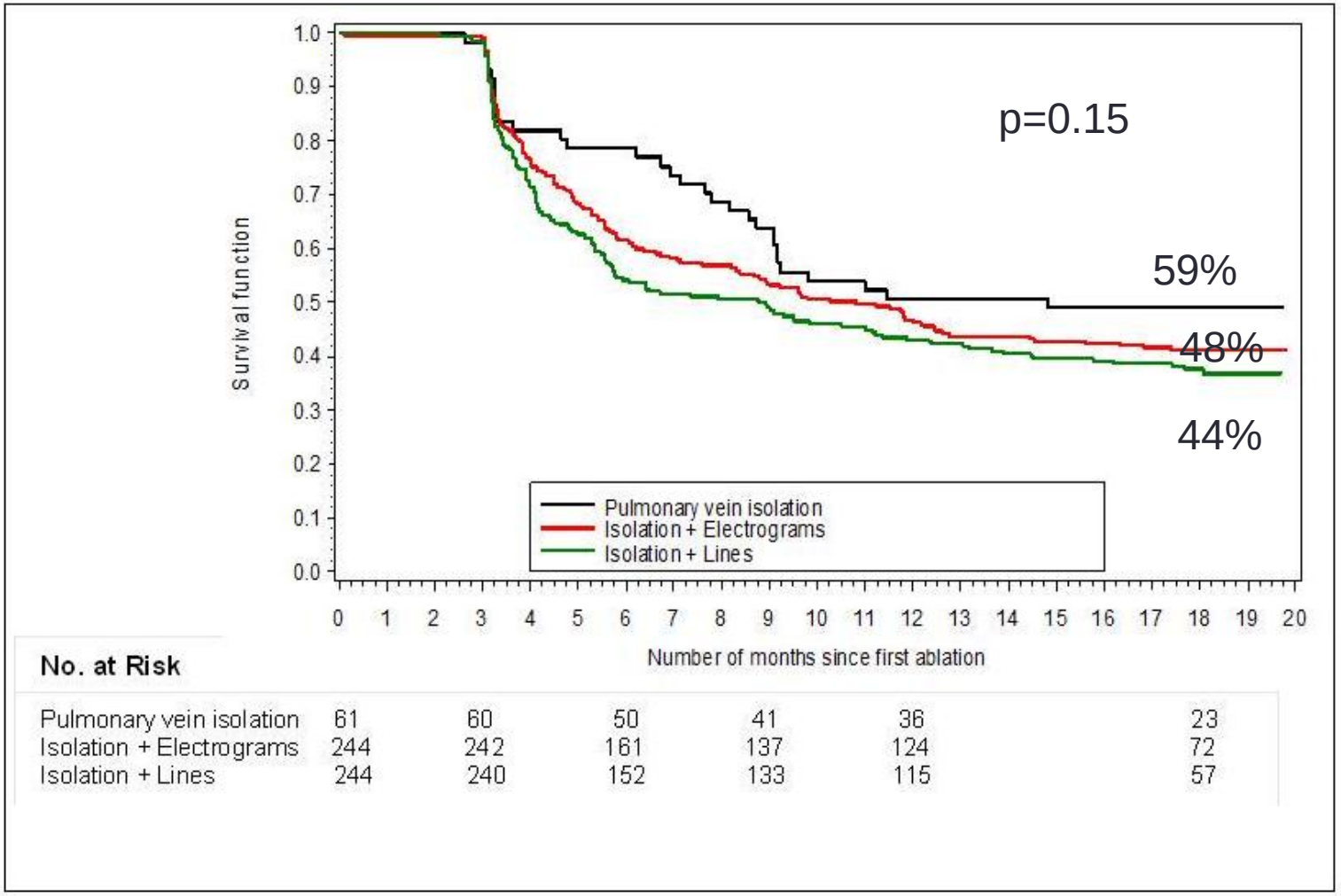
STAR-AF II: Results – Procedural Characteristics

mean time (min)	PVI	PVI+CFE	PVI+LINES	p value
Procedure	167	229	222	<0.0001
Mapping	14	18	14	<0.0001
Fluoroscopy	29	42	41	0.0003

Verma A et al, ESC 2014

STAR-AF II: Results - Primary Outcome

Documented AF > 30 seconds after <u>one</u> procedure with or without AAD



Verma A et al, ESC 2014

STAR-AF II: Results - Secondary Outcomes

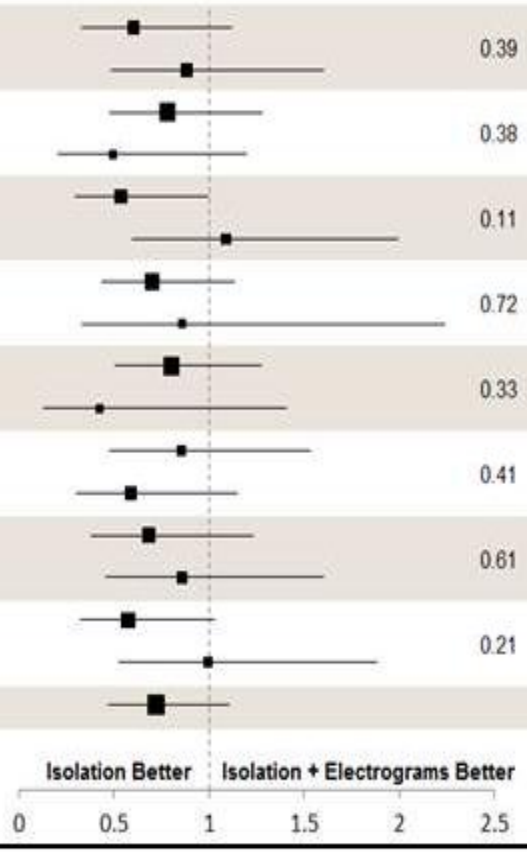
	PVI	PVI+CFE	PVI+LINES	p value
Freedom from AF/AFL/AT after 1 procedure	49 %	41 %	37 %	0.15
Freedom from AF after 2 procedures	72 %	60 %	58 %	0.18
Freedom from AF/AFL/AT after 2 procedures	60 %	50 %	48 %	0.24
Percentage of patients still on AAD at 18 mo	11 %	12 %	12 %	0.35

* AAD = antiarrhythmic drug

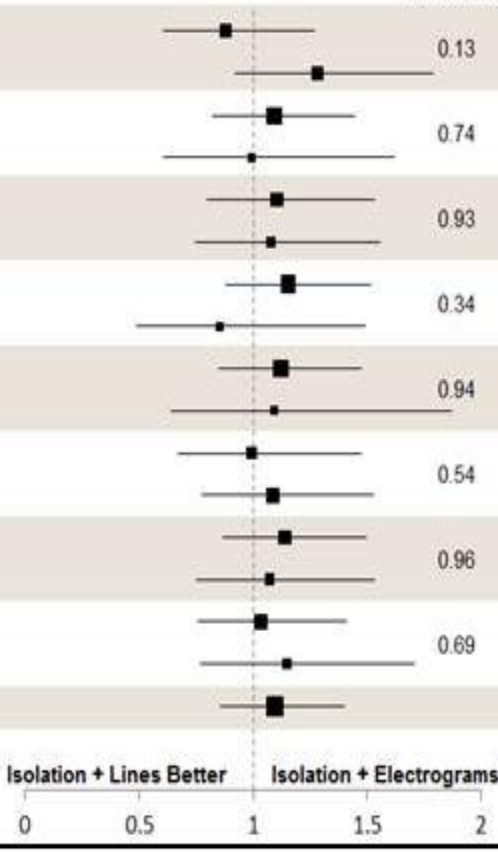
Verma A et al, ESC 2014

STAR-AF II: Results - Subgroups

Subgroup		Patients *total no.*	PVI	PVI+CFE	PVI+LINES	p for interaction	p for interaction
Age	≤ 60 yr	264	64.57	47.16	52.55	0.39	0.13
	> 60 yr	285	51.85	48.38	37.87		
Gender	Male	430	59.5	50.22	47.15	0.38	0.74
	Female	119	57.14	37.16	34.36		
BMI	≤ 29 kg/m^2	322	69.03	50.55	46.00	0.11	0.93
	> 29 kg/m^2	227	40.91	43.49	42.14		
$CHADS_2$ score	0 or 1	455	60.72	50.48	44.11	0.72	0.34
	>1	94	50.00	32.33	44.80		
Constantly in AF	Yes	416	53.01	45.94	41.31	0.33	0.94
	No	133	78.57	54.52	51.63		
LVEF	≤ 55%	201	48.15	40.13	41.51	0.41	0.54
	> 55%	326	68.61	53.76	47.25		
LA size	≤ 45mm	302	62.73	50.83	47.42	0.61	0.96
	> 45mm	242	50.00	43.54	40.23		
AAD at last follow up	OFF	371	68.88	51.12	49.71	0.21	0.69
	ON	178	36.84	40.01	34.34		
Overall		549	58.92	47.75	44.17		



PVI vs. PVI+CFE



PVI+Lines vs. PVI+CFE

Verma A et al, ESC 2014

STAR-AF II: Conclusions

- Largest randomized trial to examine outcomes of catheter ablation in persistent AF
- Additional CFE or Lines ablation increased procedural time (may increase risk)
- No benefit in AF reduction when additional substrate ablation (CFE or Lines) was performed in addition to PVI
- PVI alone achieved freedom from recurrence in about 50% of patients – comparable to published success rates from randomized, multicenter trials in paroxysmal AF
- **Where do we go from here?**

New Ablation Tools

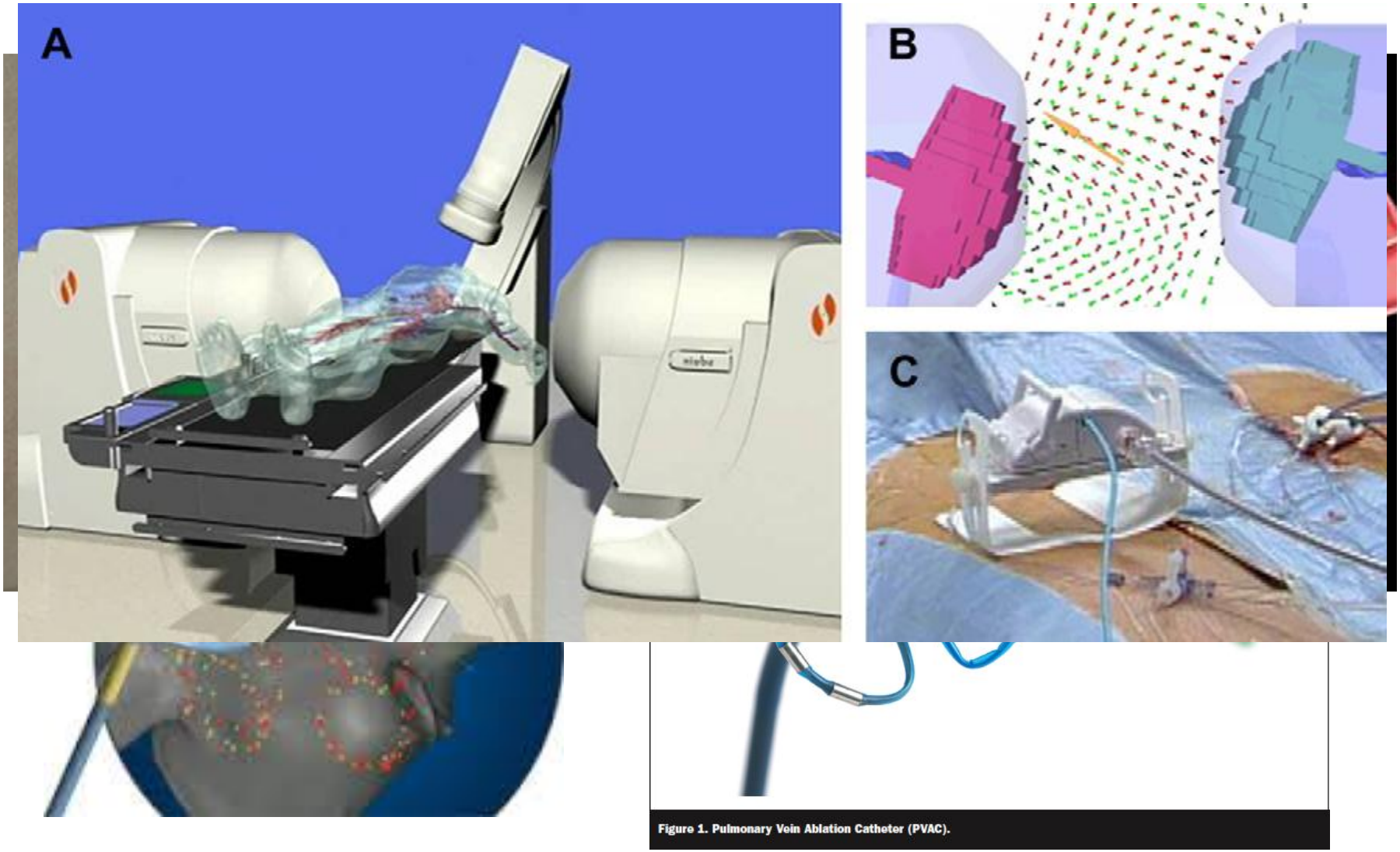
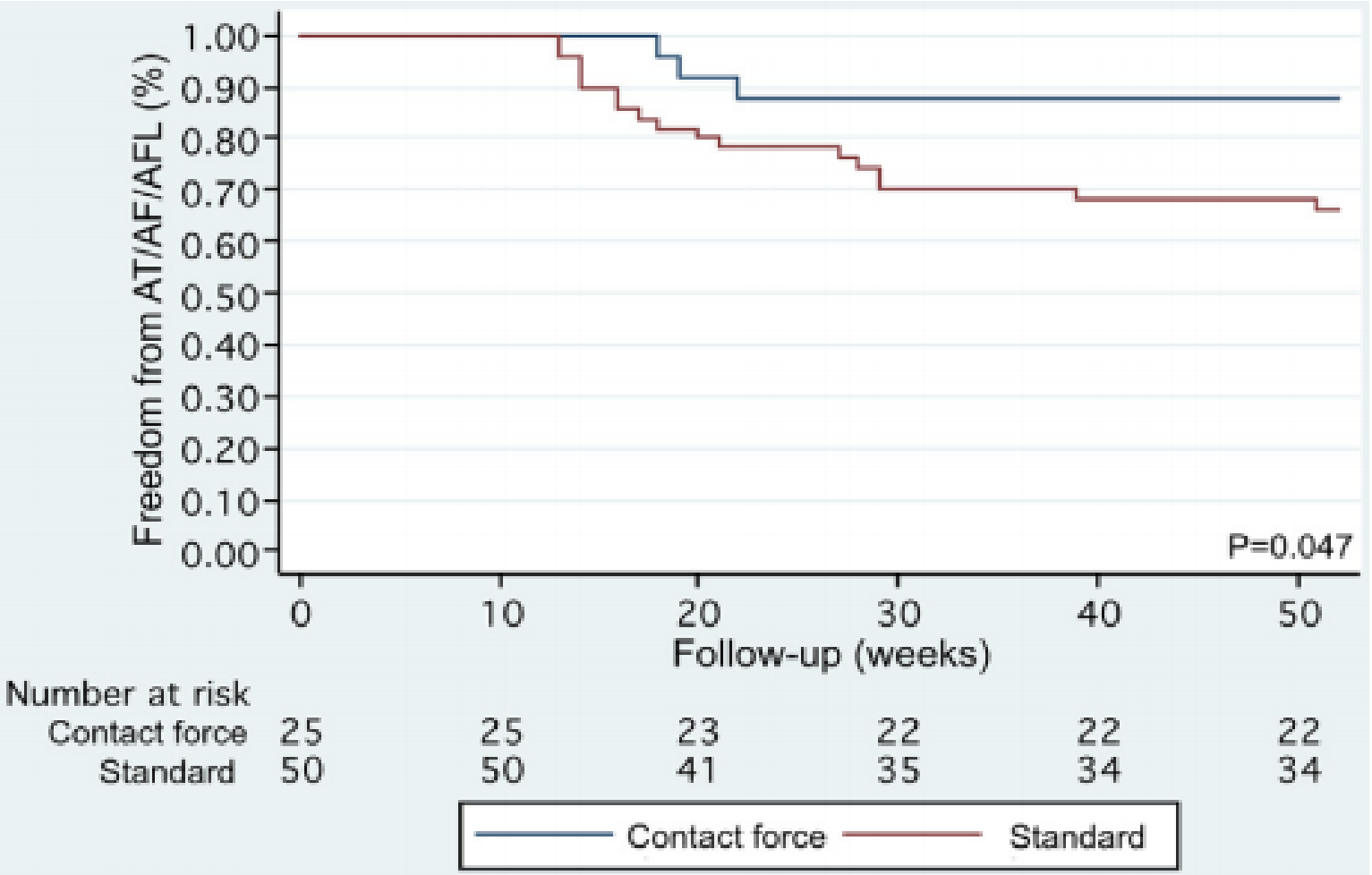


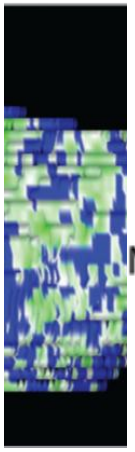
Figure 1. Pulmonary Vein Ablation Catheter (PVAC).

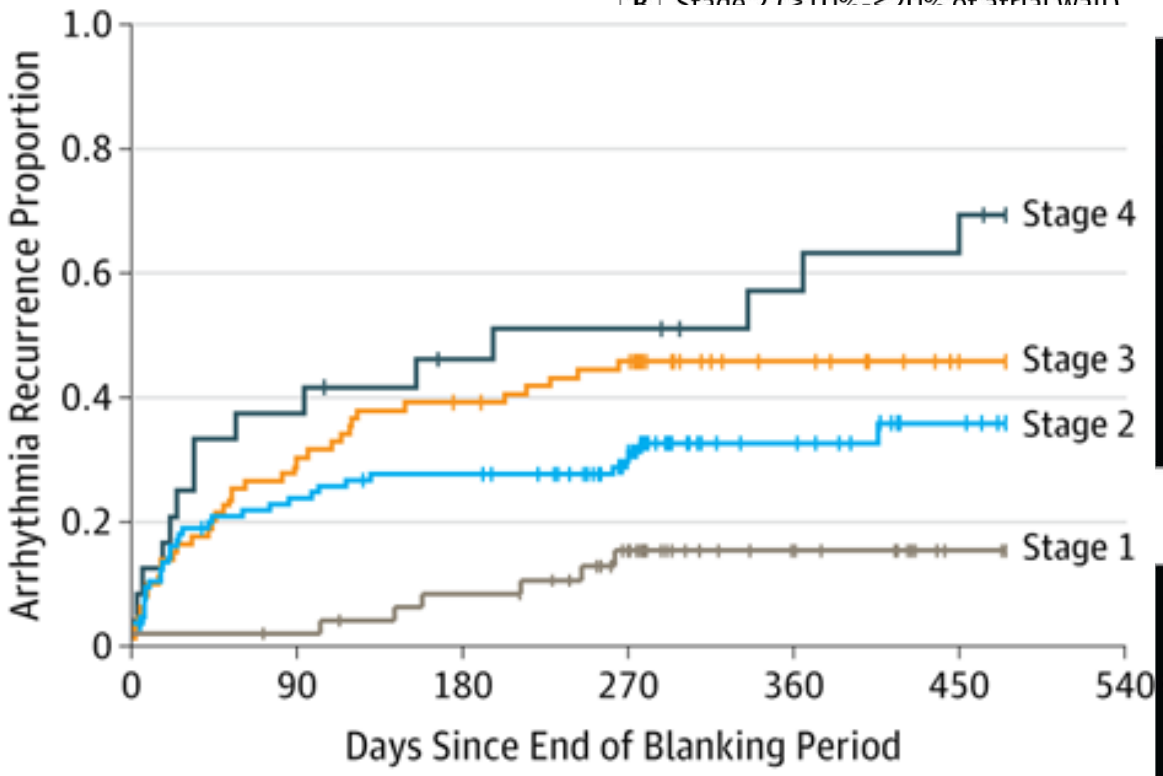
Contact Force Guided Ablation

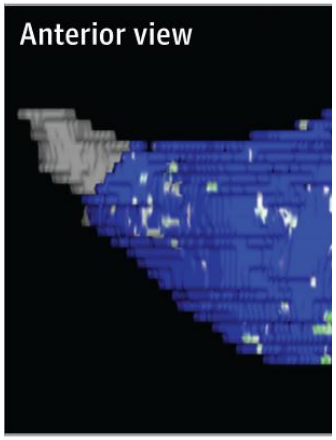


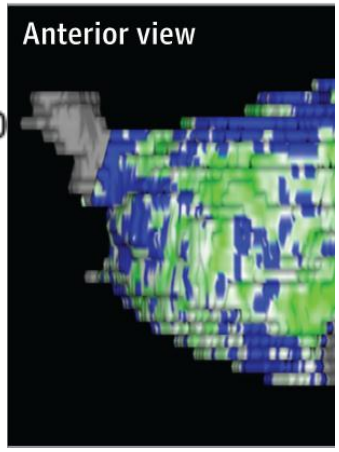
Andrade JC et al Heart Rhythm 2014

Atrial Scarring by MRI and AF Recurrence





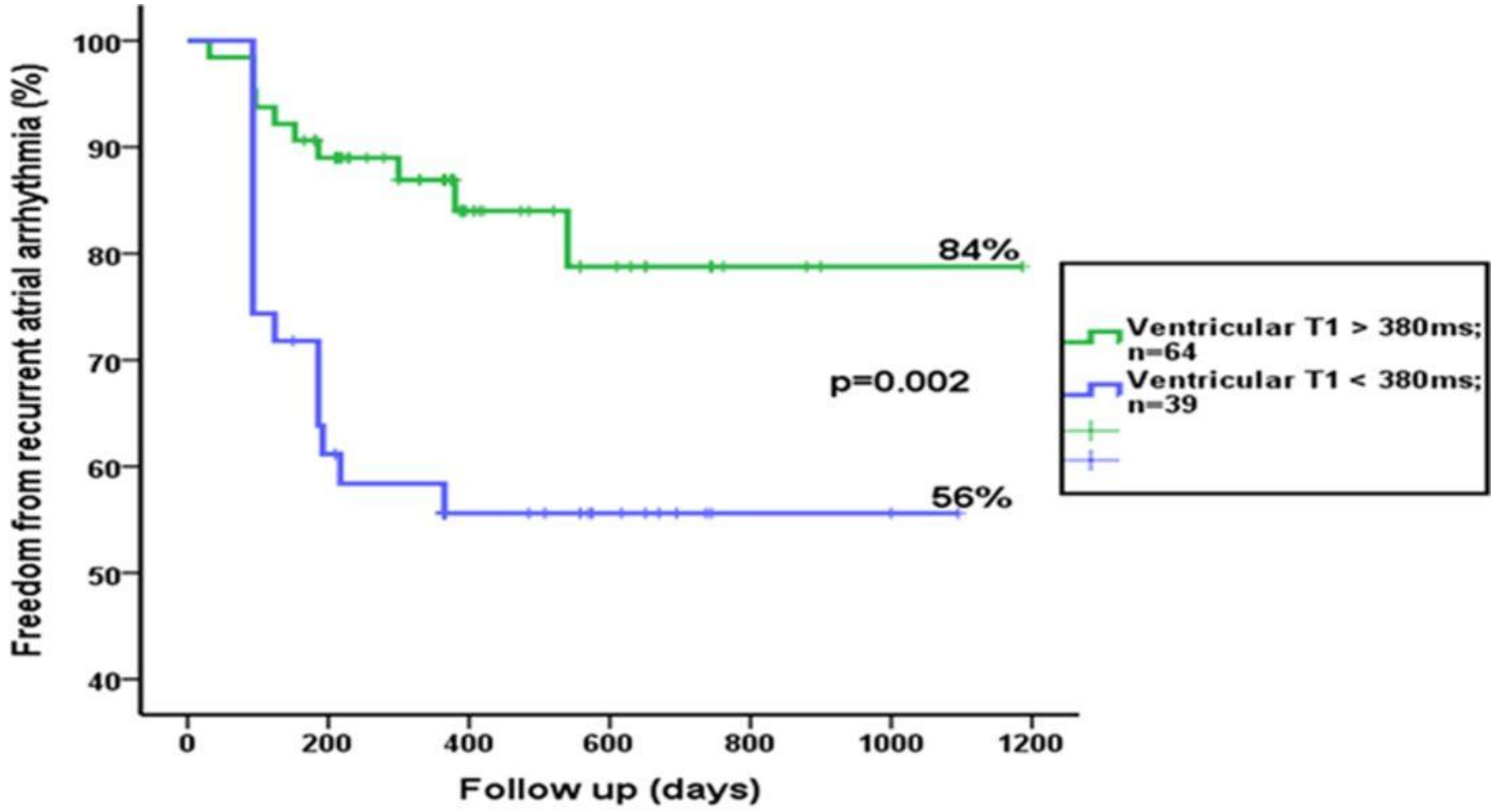




No. at risk						
Stage 1	24	15	11	10	7	6
Stage 2	80	56	47	41	19	12
Stage 3	107	79	74	58	26	15
Stage 4	49	47	43	33	13	4

Marrouche NF, JAMA 2014

Ventricular Diastolic Dysfunction by MRI and AF Recurrence



Number at Risk

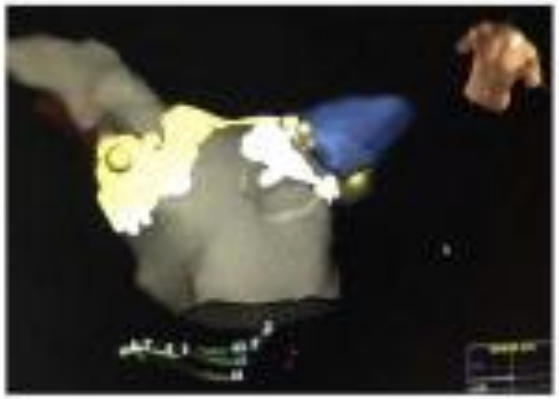
	Days					
	0	200	400	600	800	1000
Ventricular T_1 > 380ms	64	54	23	11	3	1
Ventricular T_1 < 380ms	39	23	13	8	2	2

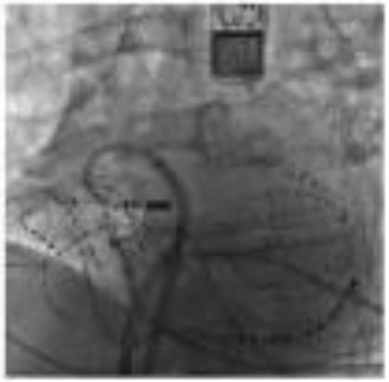
McLellan A J et al. Circ Arrhythm Electrophysiol. 2014

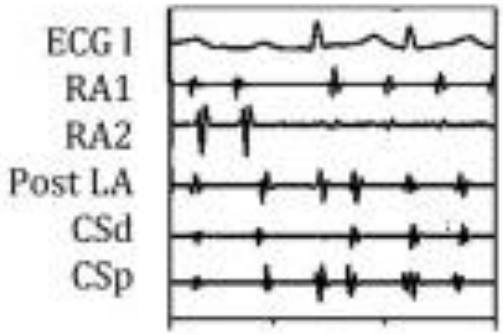
Focal Impulse and Rotor Modulation (FIRM)

A

AF Despite WACA/Roof Line, Mapped by FIRM

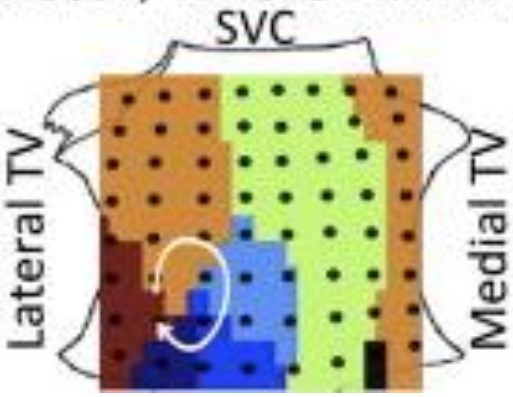






B

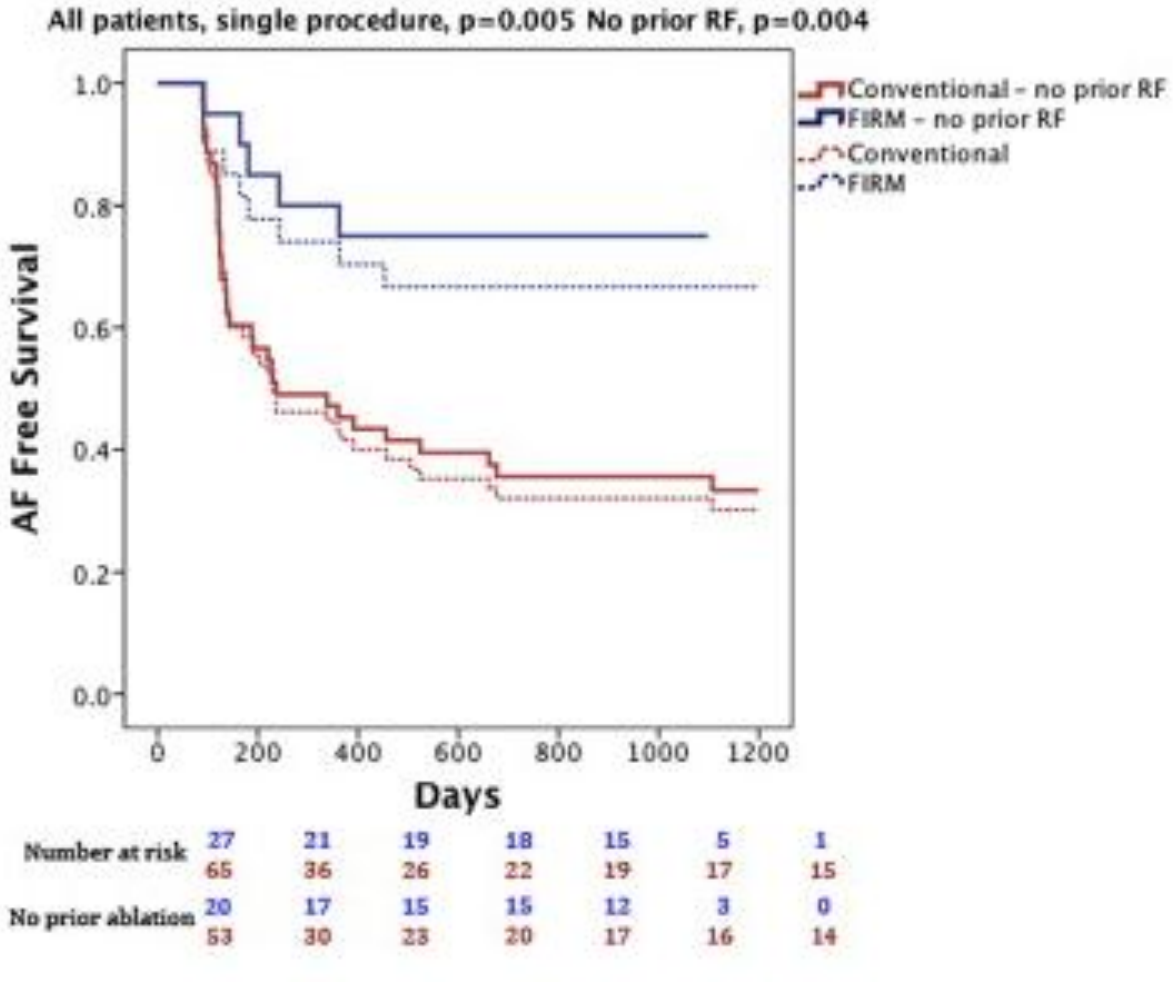
RA Rotor, Where FIRM Ablation Eliminates AF



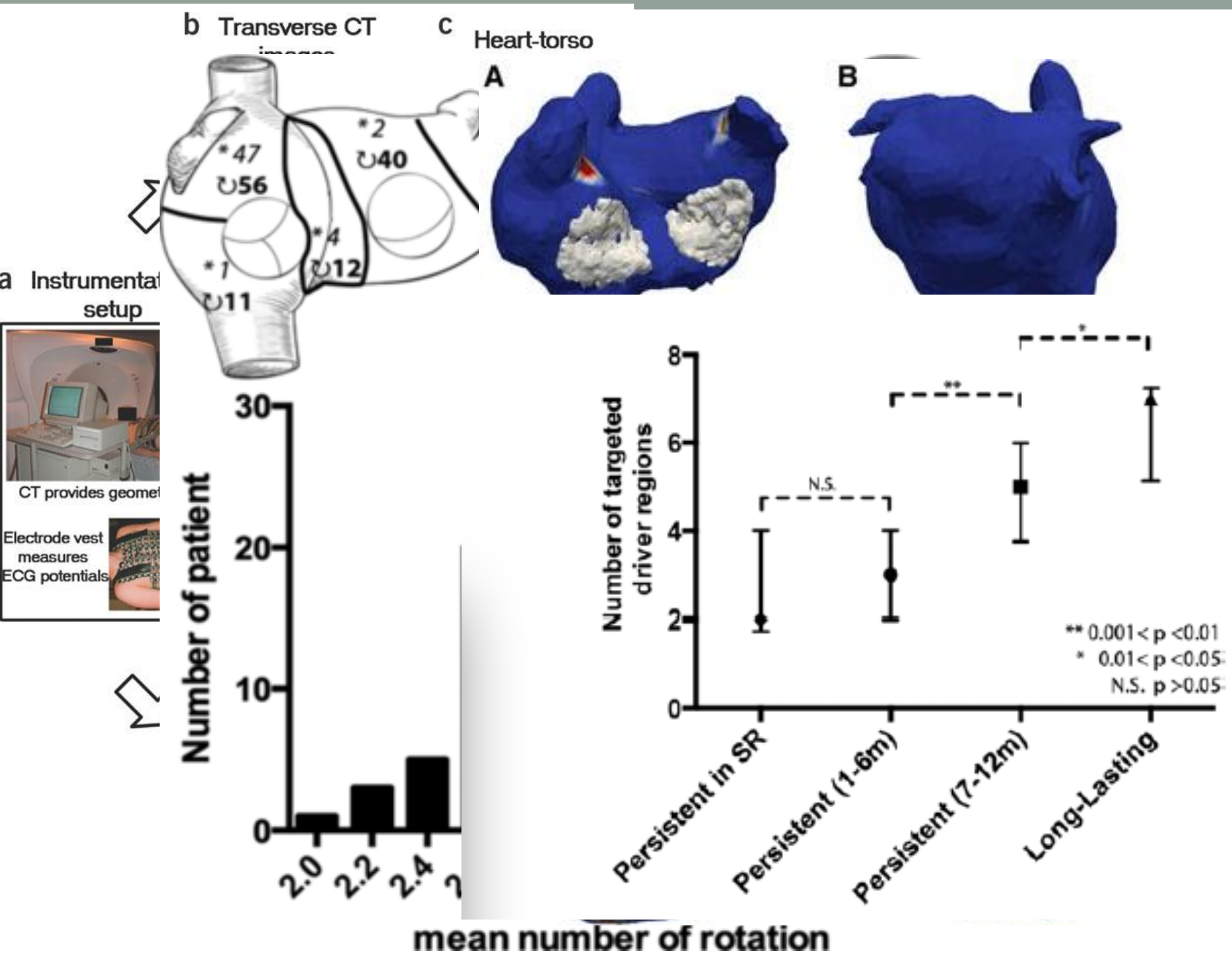
Narayan S, JACC 2014

Ablation of Rotor and Focal Sources Reduces Late Recurrence of Atrial Fibrillation Compared With Trigger Ablation Alone

Extended Follow-Up



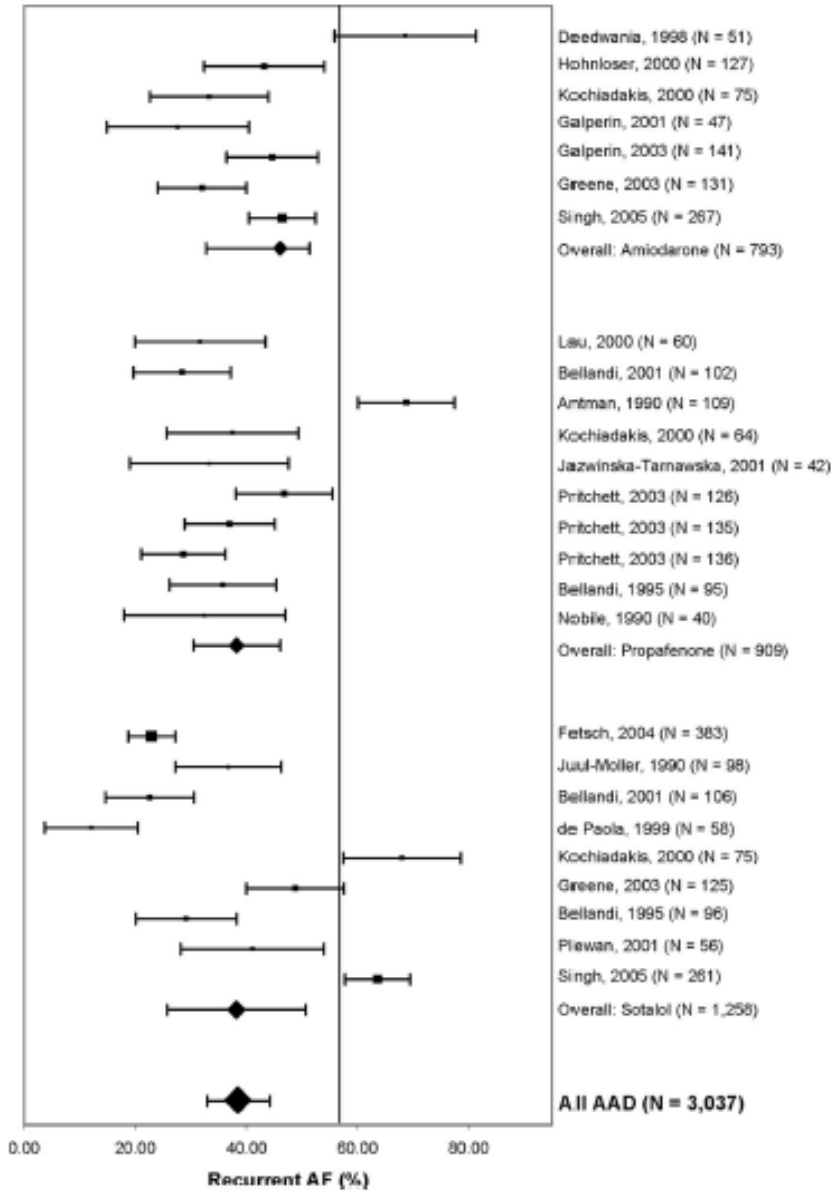
Narayan S, JACC 2014



Haissaguerre M, circulation 2014

Efficacy of AADs

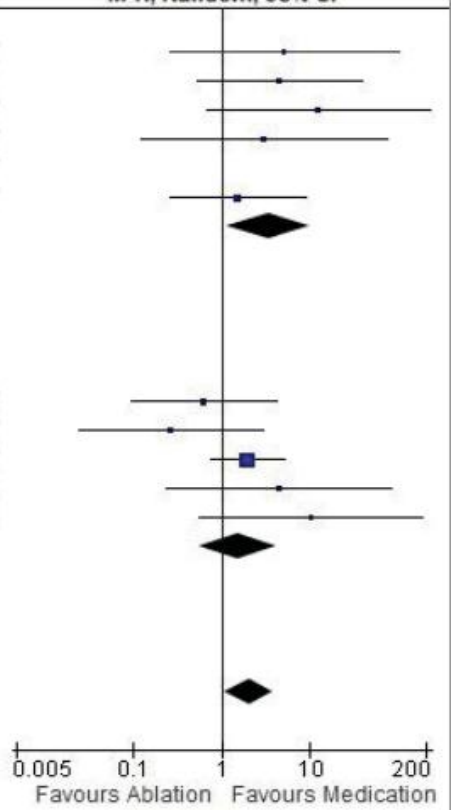
OR of Amiodarone vs. placebo = 6.1



Calkins H, et al. Circ EP 2009

Safety of Catheter Ablation to AADs

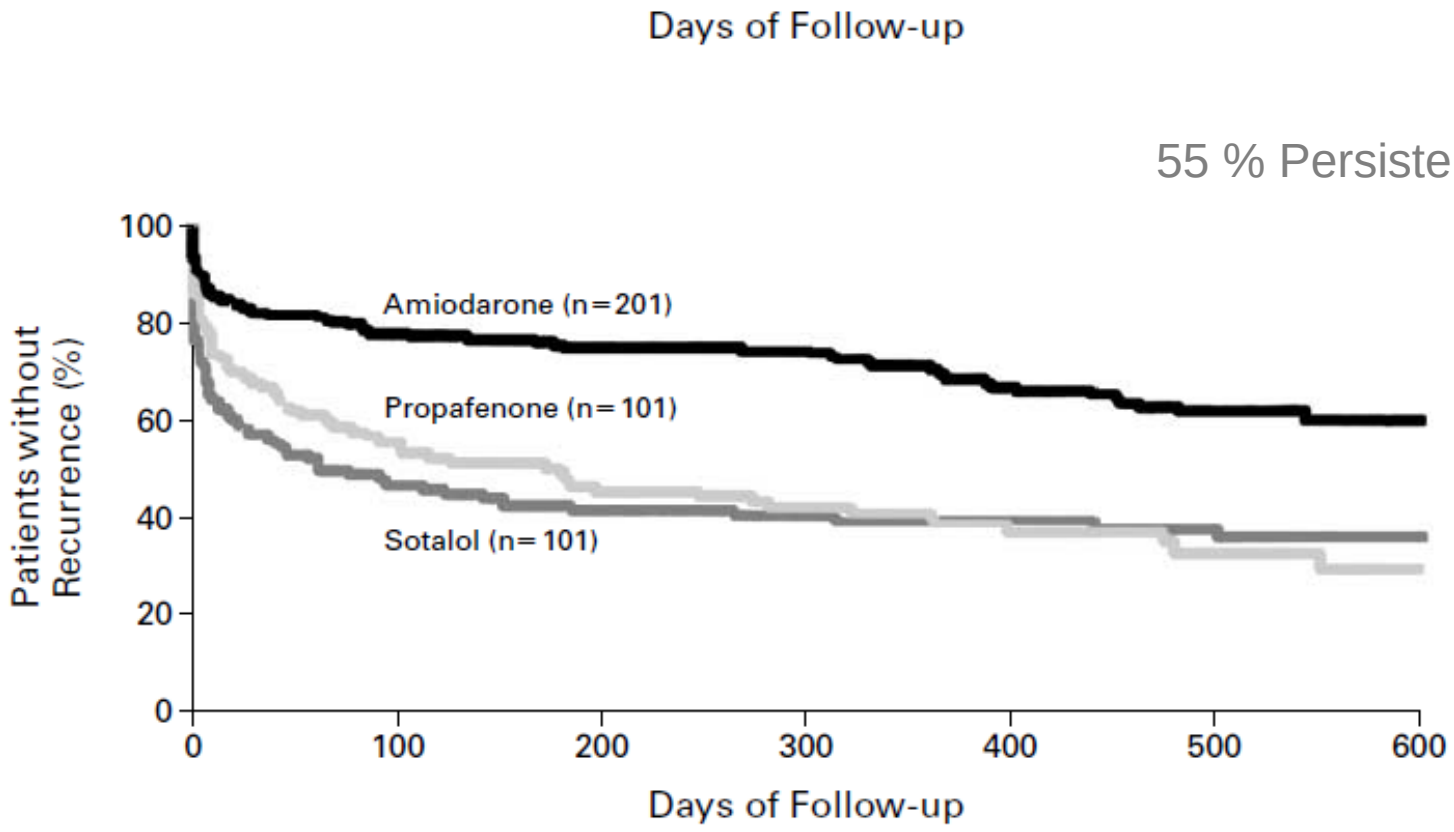
Study or Subgroup	Catheter Ablation Events	Total	Anti-arrhythmic Drugs Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
2.2.1 Early Studies (Before 2009)							
Krittayaphong 2003	2	15	0	15	4.3%	5.00 [0.26, 96.13]	2003
Wazni 2005	4	33	1	37	8.3%	4.48 [0.53, 38.14]	2005
Jais 2008	5	53	0	59	4.6%	12.22 [0.69, 215.91]	2006
Pappone 2006	1	99	0	99	3.7%	3.00 [0.12, 72.76]	2006
Oral 2006	0	77	0	69		Not estimable	2006
Stabile 2006	3	68	2	69	12.3%	1.52 [0.26, 8.83]	2006
Subtotal (95% CI)		**345**		**348**	**33.2%**	**3.35 [1.15, 9.75]**	
Total events	15		3				
Heterogeneity: Tau² = 0.00; Chi² = 1.77, df = 4 (P = 0.78); I² = 0%							
Test for overall effect: Z = 2.22 (P = 0.03)							
2.2.2 Later Studies (After 2009)							
Forleo 2009	2	35	2	22	10.6%	0.63 [0.10, 4.14]	2009
Wilber 2010	1	103	2	56	6.7%	0.27 [0.03, 2.93]	2010
Nielsen 2012	11	138	6	148	40.4%	1.97 [0.75, 5.17]	2012
Mont 2014	4	98	0	48	4.5%	4.45 [0.24, 81.09]	2014
Morillo 2014	5	66	0	61	4.6%	10.18 [0.57, 180.32]	2014
Subtotal (95% CI)		**440**		**335**	**66.8%**	**1.51 [0.55, 4.15]**	
Total events	23		10				
Heterogeneity: Tau² = 0.36; Chi² = 5.44, df = 4 (P = 0.24); I² = 27%							
Test for overall effect: Z = 0.80 (P = 0.42)							
Total (95% CI)		**785**		**683**	**100.0%**	**2.04 [1.10, 3.77]**	
Total events	38		13				
Heterogeneity: Tau² = 0.00; Chi² = 8.50, df = 9 (P = 0.48); I² = 0%							
Test for overall effect: Z = 2.27 (P = 0.02)							
Test for subgroup differences: Chi² = 1.13, df = 1 (P = 0.29), I² = 11.2%							



Khan AR, Circ Arrhythm Electrophysiol 2014

Amiodarone vs other AADs

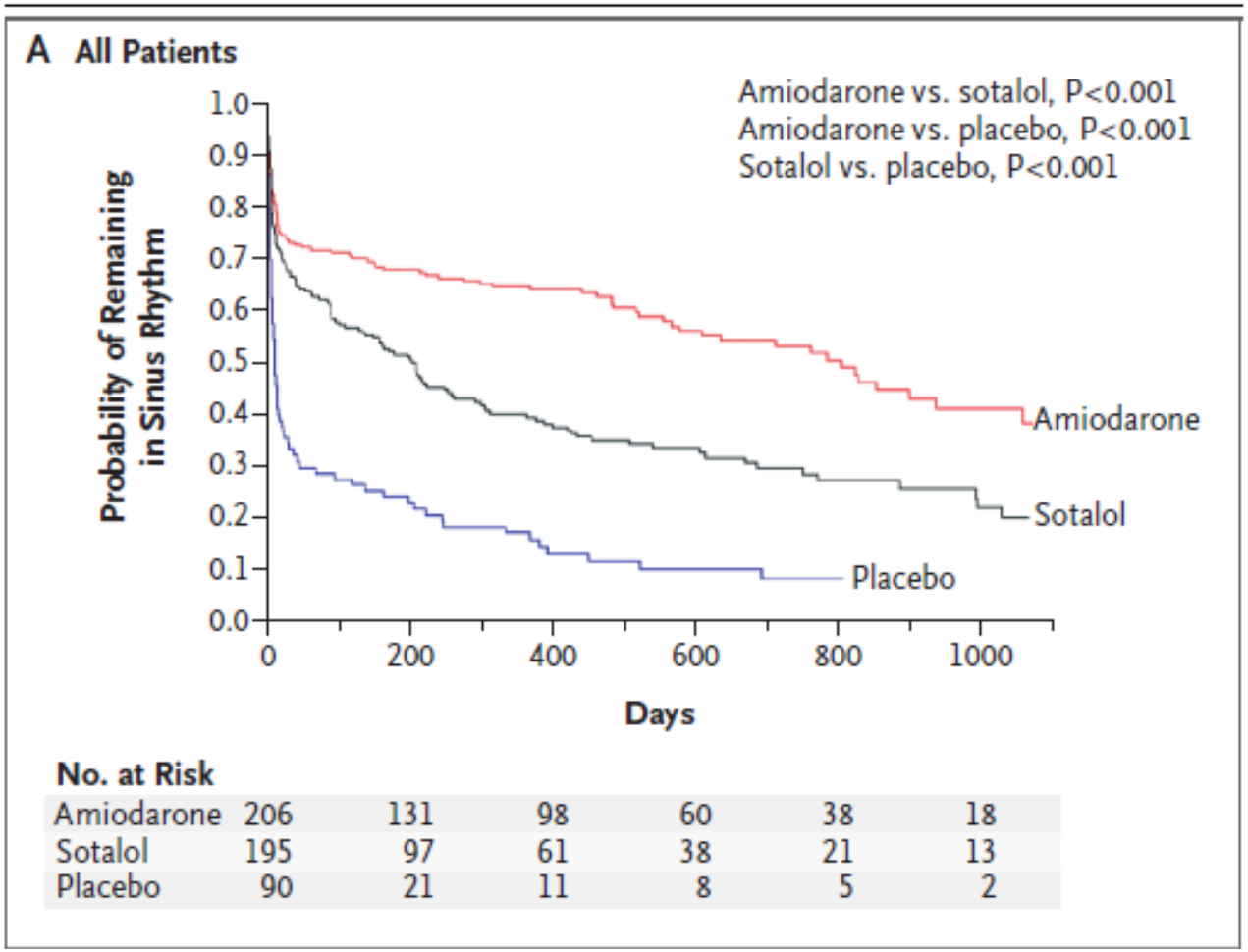
55 % Persistent AF



Roy D, et al. NEJM 2000

SAFE-T

- All Pers. AF
- 22% >1 yr

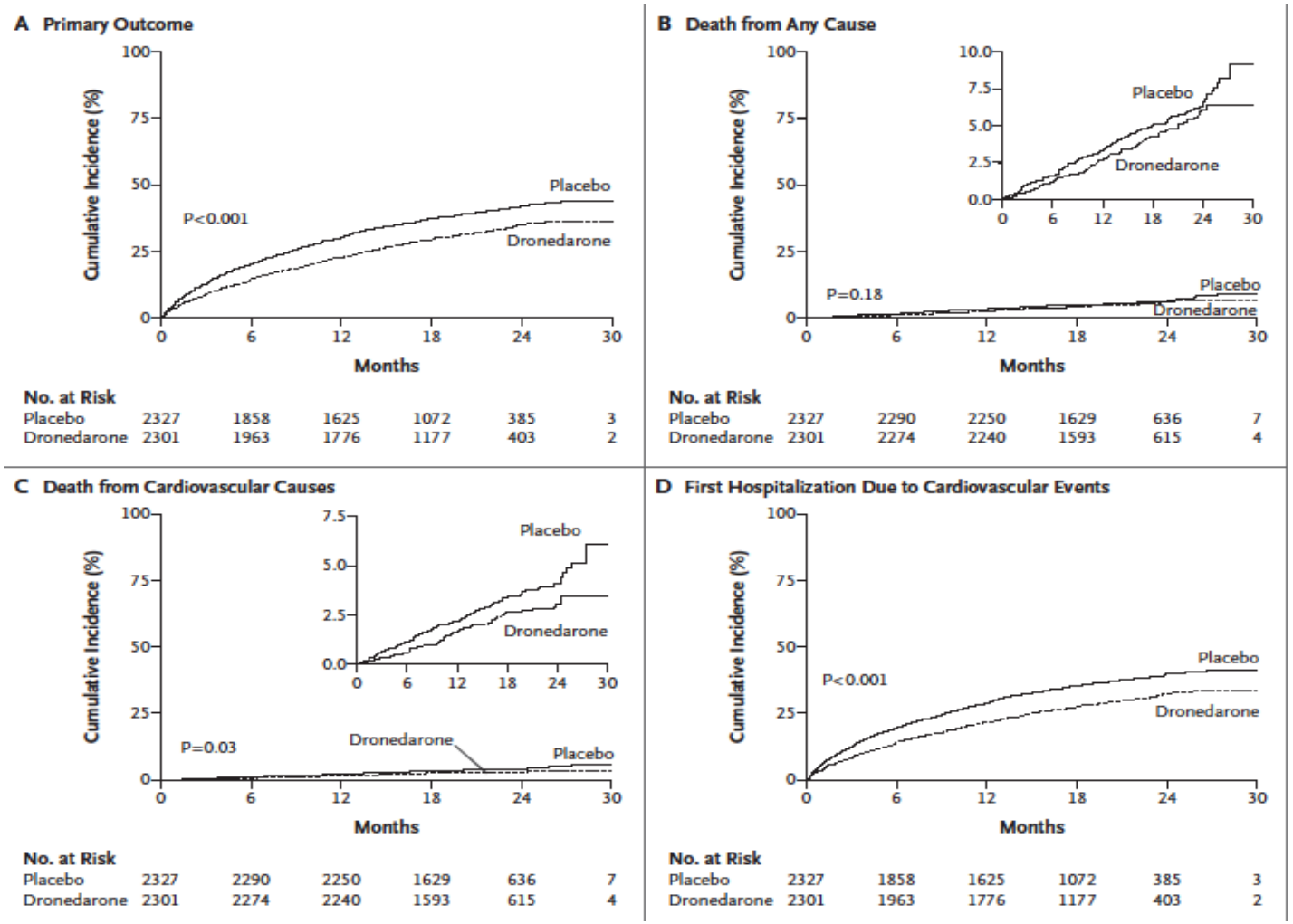


Singh BN, NEJM 2005

STUDY OUTCOMES

The primary study outcome was the first hospitalization due to cardiovascular events or death from any cause. Any unplanned hospitalization (i.e., admission with an overnight stay in the hospital) was classified by the investigator as a hospitalization due to either cardiovascular or noncardiovascular causes.[11] Deaths were categorized by means of blinded adjudication, according to a modified Hinkle and Thaler classification,[12] into four categories: death from cardiac arrhythmia, death from nonarrhythmic cardiac causes, death from noncardiac vascular causes, and death from noncardiovascular causes. This classification scheme

ATHENA



Hohnloser S, NEJM 2009

Conclusions

- Ablation for Persistent. AF- LESS IS BETTER.
  - No obvious advantage for anything more than PVI
- Better patient selection:
  - Incorporating MRI, other markers
- Understand the pathophysiology:
  - Rotor identification and ablation
- Accept limitations of ablating non-paroxysmal AF:
  - Rethink AAD- mainly Amiodarone
- Paradigm Shift:
  - Focus on symptoms/ QOL / Hospital admissions and not upon AT/AF recurrence

Thank you