ΥΠΟΤΡΟΠΗ ΚΟΛΠΙΚΗΣ ΜΑΡΜΑΡΥΓΗΣ ΚΑΤΟΠΙΝ ABLATION:

Επανάληψη, φάρμακα ή χειρουργική επέμβαση?

Δημοσθένης Κατρίτσης

ΕΥΡΩΚΛΙΝΙΚΗ Αθηνών

2012

Post-ablation AF Recurrence

Lemery R. Europace 2011;13:301-3

Table I Long term success rates in 1894 patients of a single radiofrequency catheter ablation procedure for paroxysmal atrial fibrillation that includes circumferential ablation of the pulmonary veins with or without non-PV sites of ablation

Study	Year	Pts (n)	Approach		Follow-up (years)	Follow-up method	Success (%)
			PVI	Non-PVI			
Bhargava et al.[7]	2009	728	PVAI	SVC, triggers	4.8 ± 1.4	48h Holter 3, 6, 9 and 12 months, event monitor during the first 5 months	77.6
Hunter et al.[8]	2010	151	WACA	–	3.3[a]	Holter at 3 and 6 months, event monitor if symptomatic, 12-lead ECG at late follow-up	40.6
Miyazaki et al.[9]	2010	452	EPVI	CTI, triggers	2.5 ± 1.2	Holter at 2, 6, 10, 14, 24, 36, 48 weeks and every 3 months, event monitor if symptomatic	67.3
Medi et al.[10]	2010	100	PVAI	–	3.3 ± 0.8	12-lead ECG and Holter at 3, 6, 9 and 12 months, event monitor every 6 months	49.0
Wokhlu et al.[11]	2010	428	PVI/WACA	CTI, triggers, lines	3.0[b]	24h Holter at 3 months, 12-lead ECG at 12 months, event monitor if symptomatic after 12 months	62.0[c]
Mikhaylov et al.[12]	2010	35	CPVI	CTI, lines	3.0 ± 0.2	24h Holter at 3, 6, 9 and 12 months, event monitor if symptomatic	65.7

CPVI, circumferential pulmonary vein isolation; CTI, cavo tricuspid isthmus ablation; EPVI, extensive pulmonary vein isolation; PVAI, pulmonary vein antral isolation; PVI, pulmonary vein isolation; SVC, superior vena cava; WACA, wide area circumferential ablation.

[a] Median follow-up (range 2.4 - 7.5 years)

[b] Median follow-up (range 1.6 - 4.1 years)

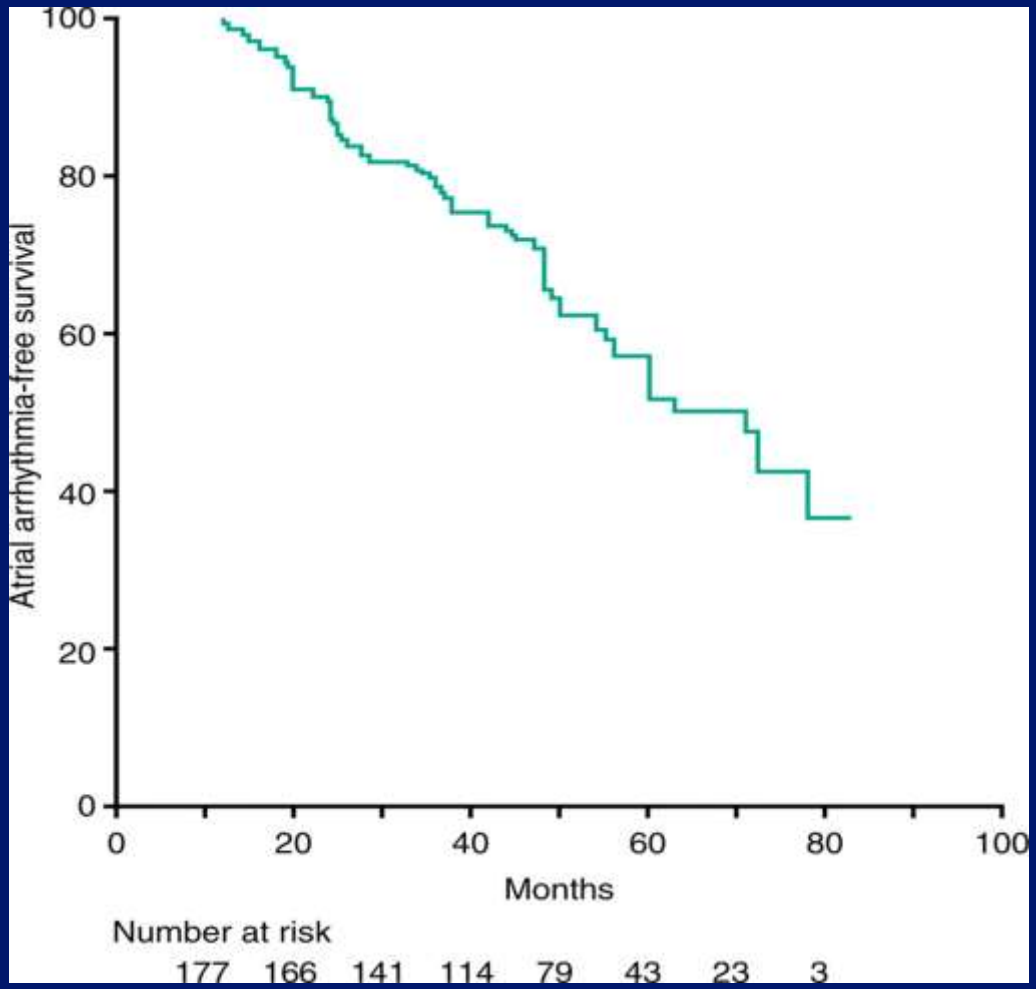
[c] At two years in 235 patients

Ablation vs Drugs for AF

A 6-year Multicentre Experience

229 pts

Bertaglia, E. et al. Europace 2009 0:eup349v1-349

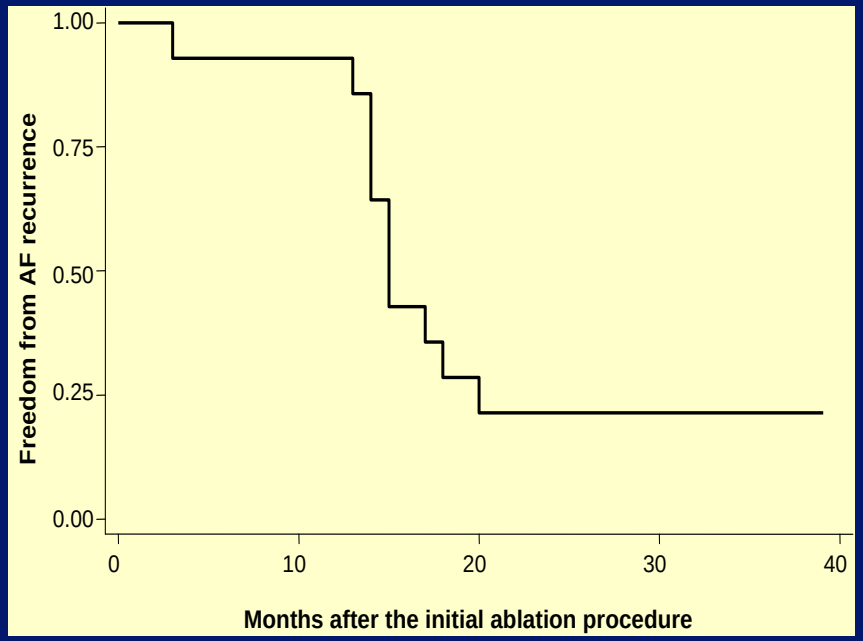


AF Ablation

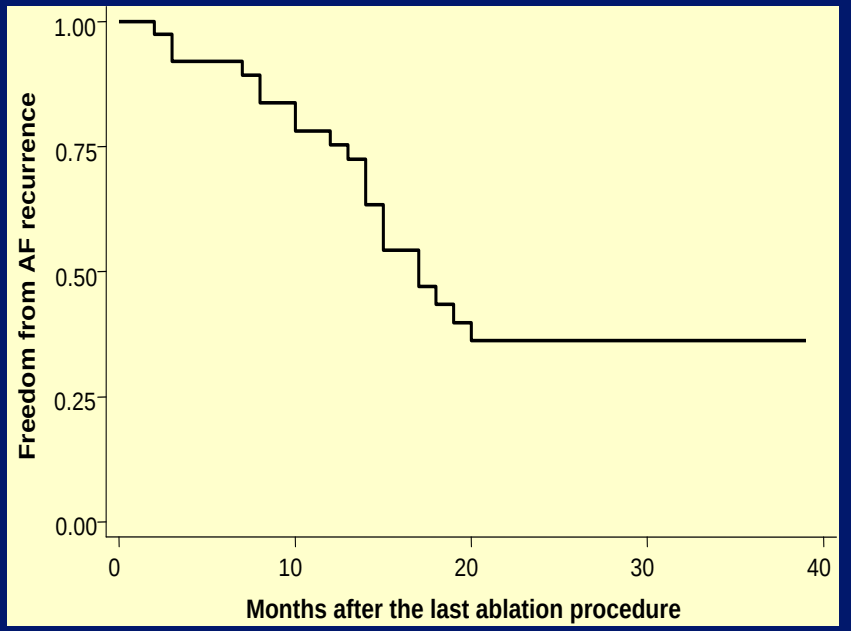
Long-term Results

Katritsis et al. Europace. 2008;10:419

39 patients with rigorous end-points and at least 3 years follow-up
14 pts (35.8%) had one, 19 pts (50%) had two,
and 6 pts (15.4%) had three ablation procedures



Freedom from AF recurrence after the initial procedure for patients subjected to a single procedure (14 pts).

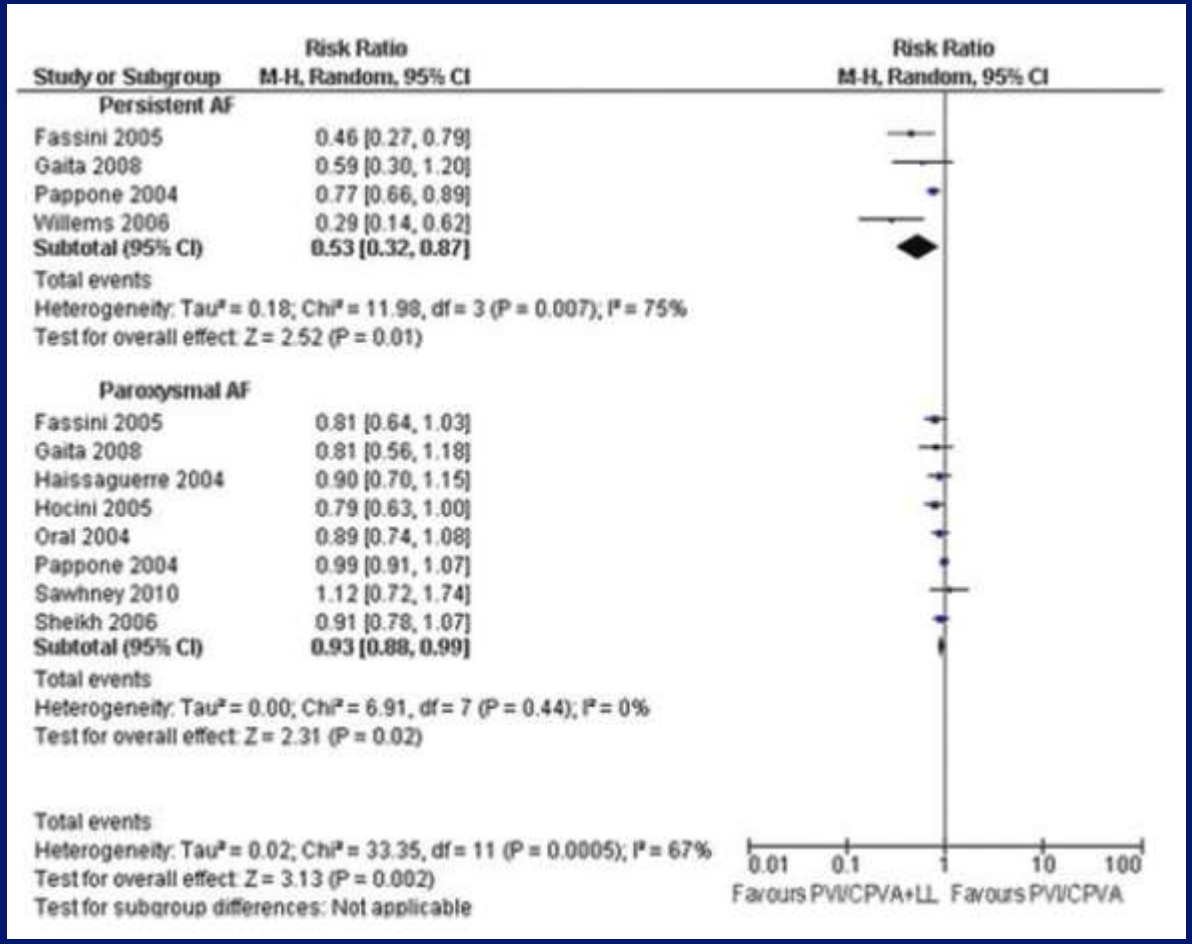


Freedom from AF recurrence after the last procedure among all patients.

Ablation for AF

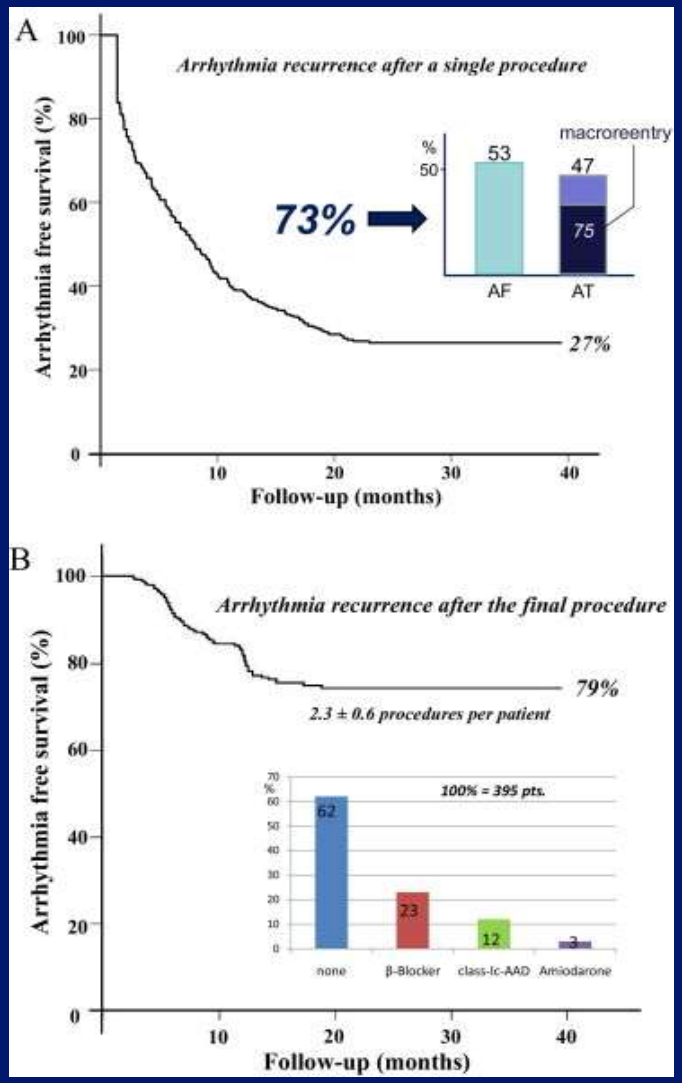
Additional Ablation for Persistent AF: a Meta-analysis of 35 RCTs

Parkash et al. JCE 2011; 22:729-738



Ablation for AF

Rostock et al. Long-term outcome after ablation of persistent AF
HeartRhythm 2011; 8:1391-1397



Drugs for AF

Randomized Studies of Rhythm vs Rate Control

PIAF
STAF
AFFIRM
RACE
AC-CHF

No motality benefit with rhythm control

Drugs for AF

Randomized Studies of Rhythm vs Rate Control

Limitations

1. Short F-U
2. ITT
3. Differences in subgroups (benefit in <50-year age)
4. QOL
   - *CTAF study (Dorian et al. Am Heart J 2002;143:984)*
5. Proarrhythmia of AAD

Drugs for AF

AADs for SR maintenance

Lafuente-Lafuente, et al. Arch Intern Med. 2006;166:719-728

Forty-four randomized trials with 11 322 patients

- Efficacy of 40-60% per year
- All increased withdrawals due to side effects
- All increasd proarrhythmia (except amiodarone and propafenone)
- Class IA increased mortality
- No mortality reduction by anyone

AADs for SR maintenance

Lafuente-Lafuente, et al. Arch Intern Med. 2006;166:719-728

Amiodarone (side-effects)

Beta blockers (reduced efficacy)

Propafenone (potentially proarrhythmic in IHD)

Flecainide (proarrhythmic in IHD)

Dofetilide (QT prolongation)

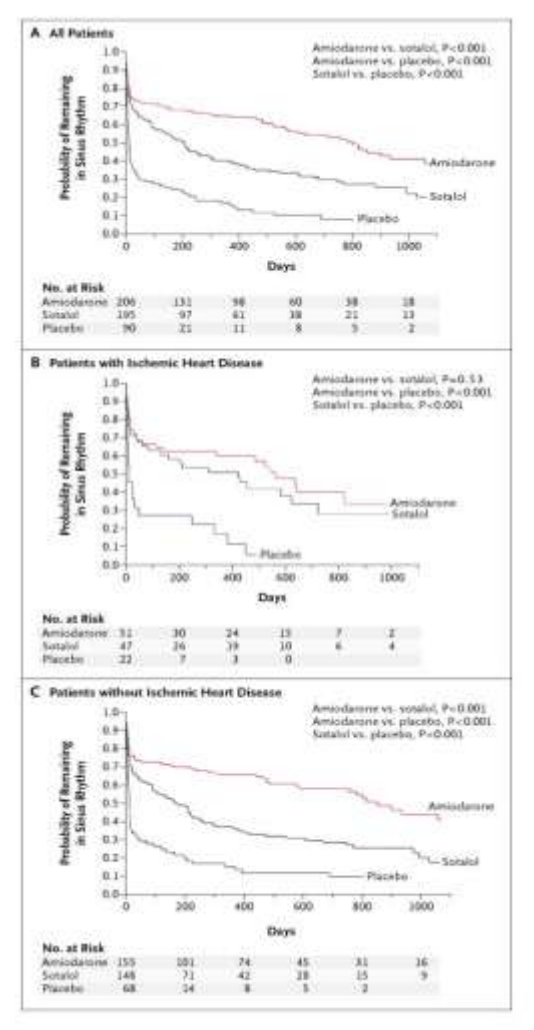
Sotalol (Increased mortality)

Dronedarone ?

Drugs for AF

Amio vs sotalol: 665 pts 1-4 years

Singh et al. N Engl J Med 2005;352:1861-1872



Kaplan-Meier s of the time to recurrence of AF among patients in whom SR was restored

13 pts died in the amiodarone group, 10 died in the sotalol group, and 2 died in the placebo group;

The death rate was 4.36 per 100 person-years of follow-up in the amiodarone and sotalol groups and 2.84 per 100 person-years of follow-up in the placebo group (P=0.13).

Drugs for AF

Class Ic AADs are proarrhythmic even in the absence of IHD

Katritsis et al. Eur Heart J 1995;16:1930

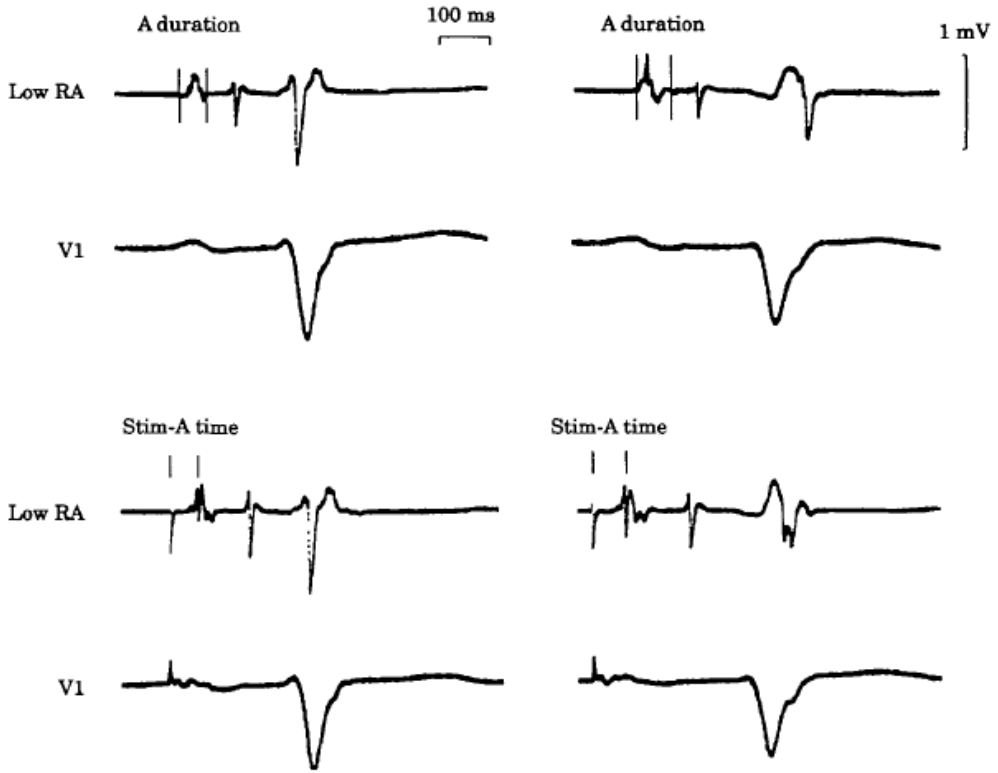


Figure 2 Atrial electrograms recorded from the low right atrium during sinus rhythm (upper panel) and high right atrial pacing at 100 ppm (lower panel), before (left) and after (right) flecainide administration. Note the widening of the atrial electrogram and the prolongation of the stimulus to A time.

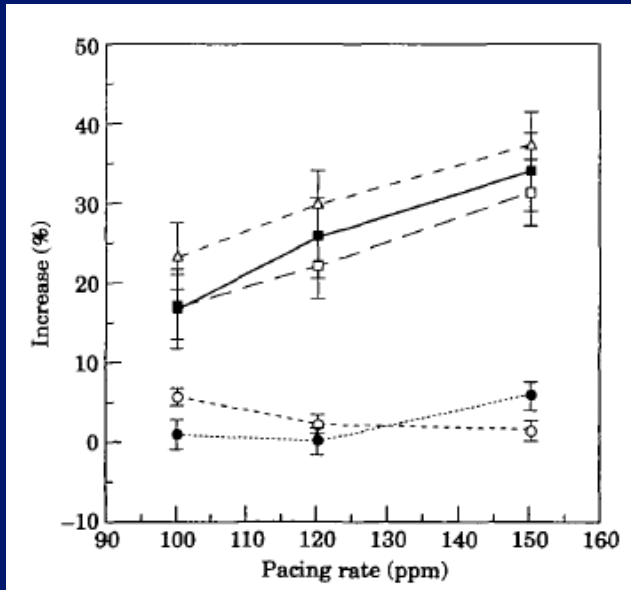


Figure 1 Regression analysis of the differences induced by flecainide in QRS duration, atrial electrogram duration, atrial refractoriness, and ventricular refractoriness as compared with pacing rate. △=stimulus to atrial electrogram time; ■=QRS duration; □=duration of atrial electrogram; ●=ventricular effective refractory period; ○=atrial effective refractory period. Values are presented as mean ± standard error of the mean.

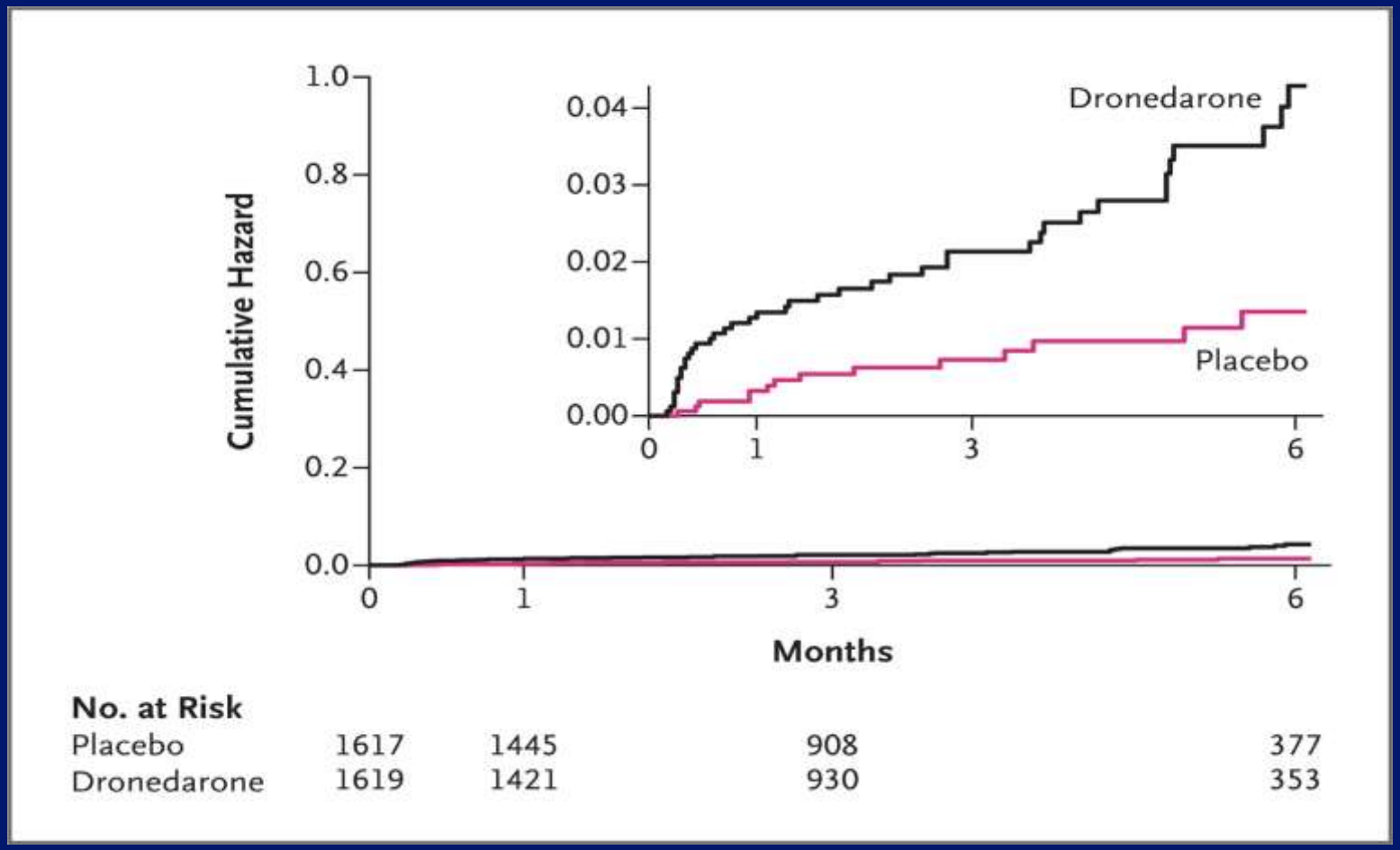
Drugs for AF

PALLAS Trial

Connolly SJ et al. N Engl J Med 2011. DOI: 10.1056/NEJMoa1109867

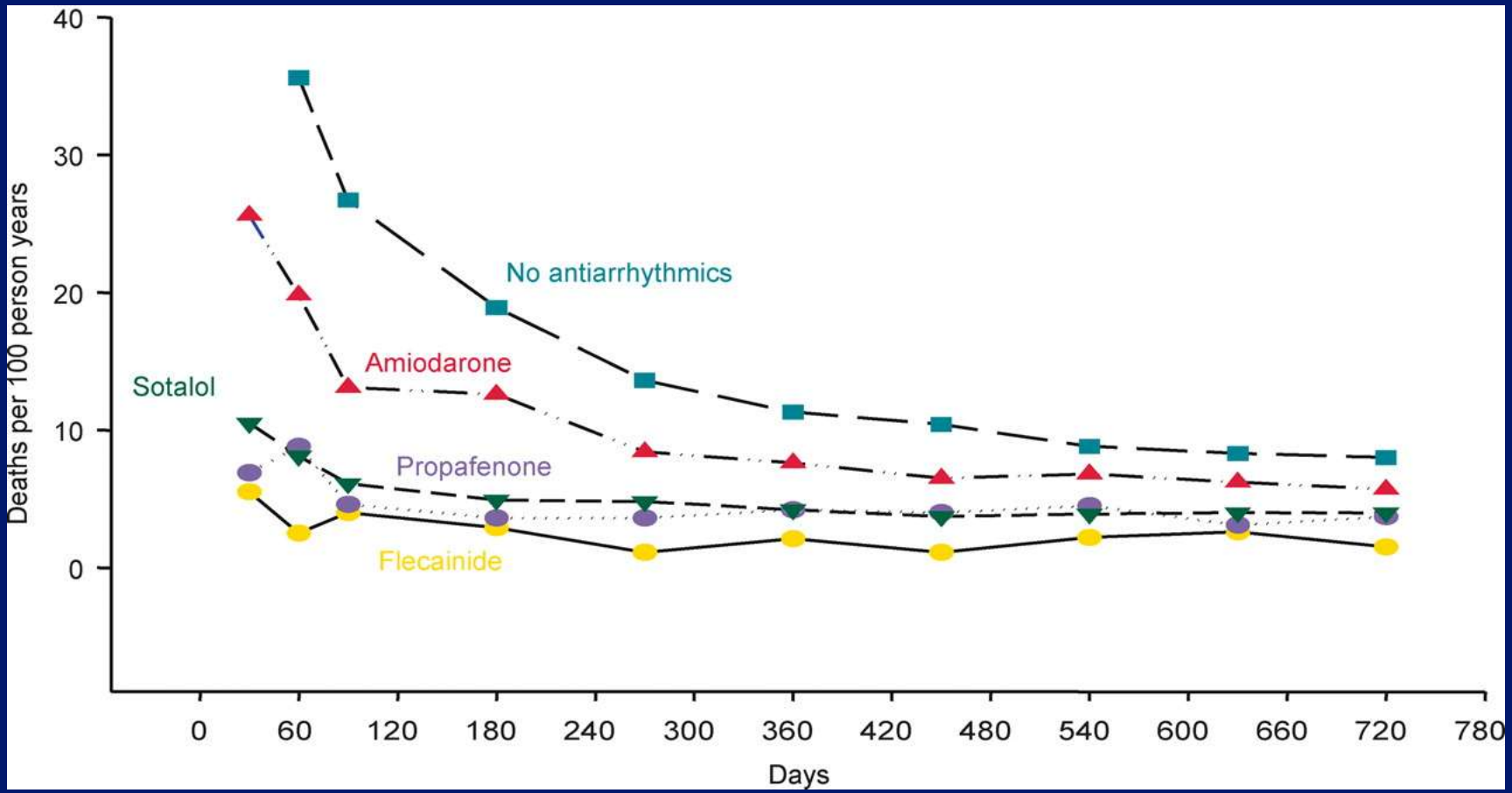
Risk of the First Coprimary Outcome

(Stroke, Myocardial Infarction, Systemic Embolism, or Death from Cardiovascular Causes)



Drugs for AF

Denmark: 1995-2004
141500 pts
Andersen et al. Europace 2009 11:886-891

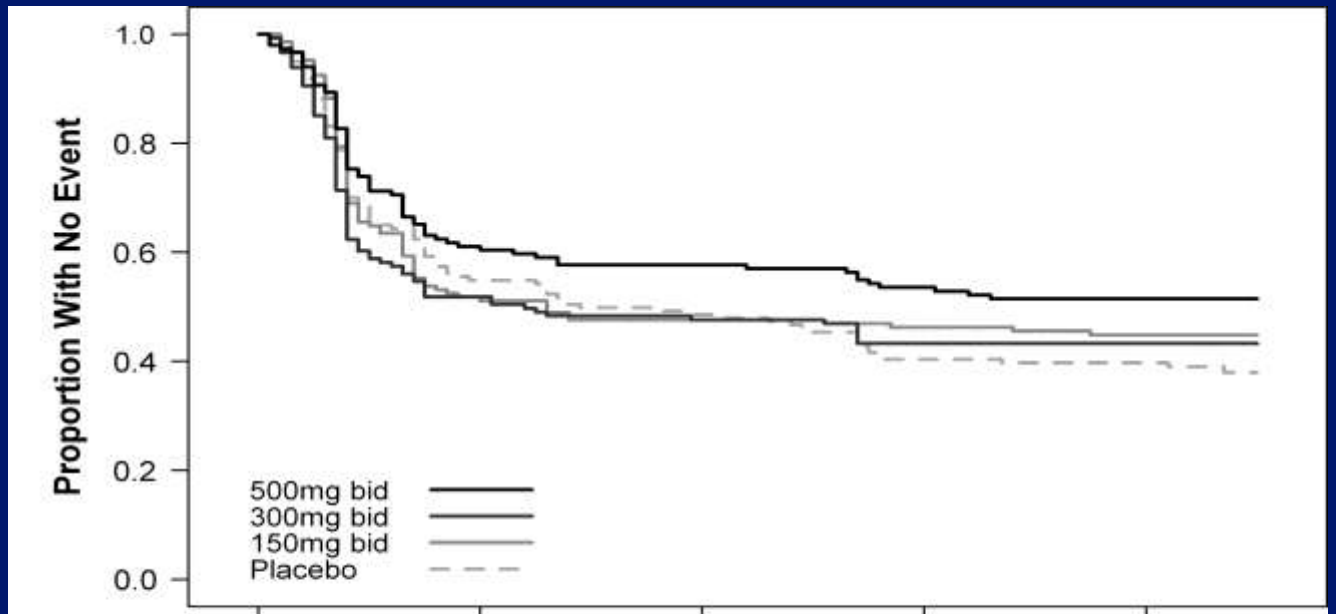


Drugs for AF

Vernakalant

Kaplan-Meier curve of time to first documented recurrence of symptomatic sustained AF

Torp-Pedersen C et al. Circ Arrhythm Electrophysiol 2011;4:637-643

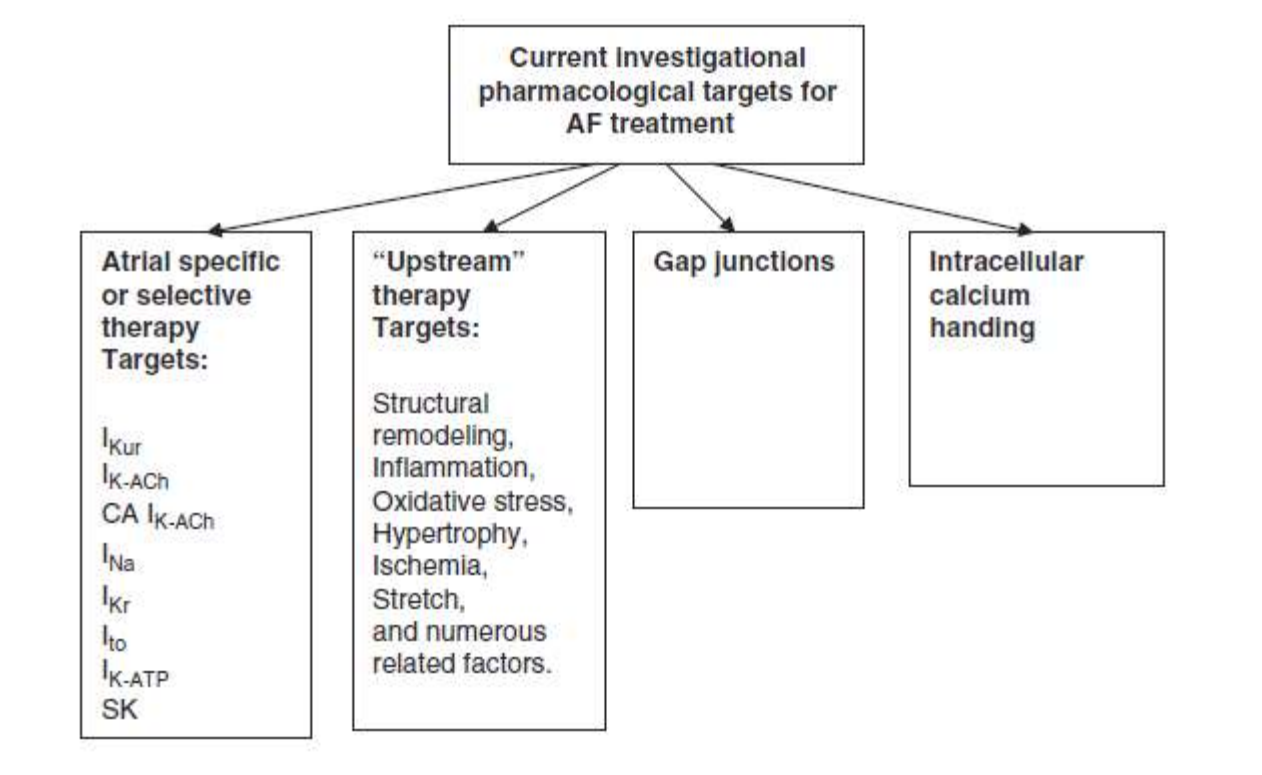


Number at Risk

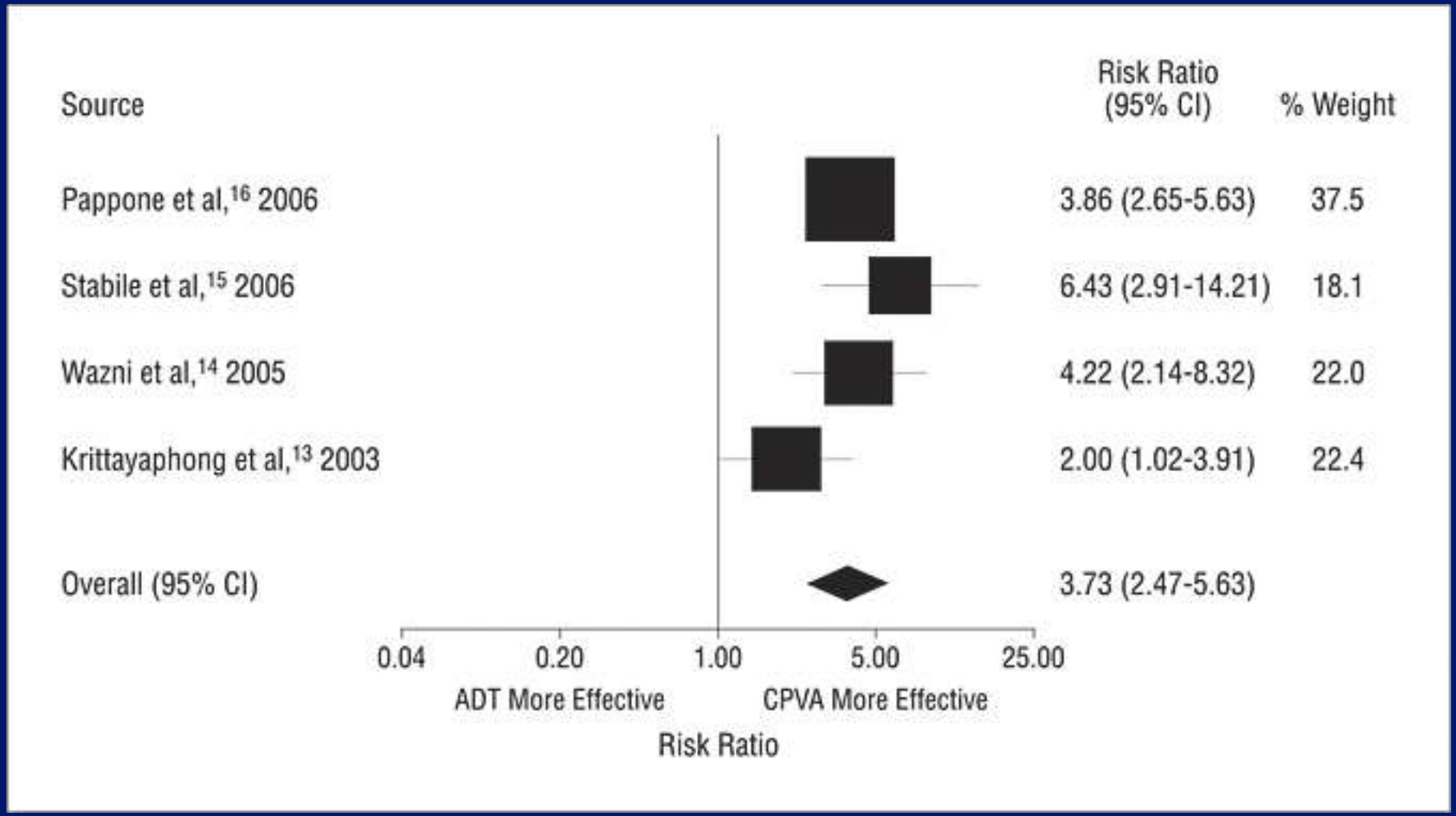
500mg bid	150	124	96	85	78	1
300mg bid	148	104	78	68	60	1
150mg bid	147	115	80	69	68	0
Placebo	160	126	99	80	64	1

New Drugs for AF

Novel pharmacological targets for the rhythm control management of AF
Burashnikov and Antzelevitch
Pharmacology and Therapeutics (E-Pub)



Ablation vs Drugs for AF

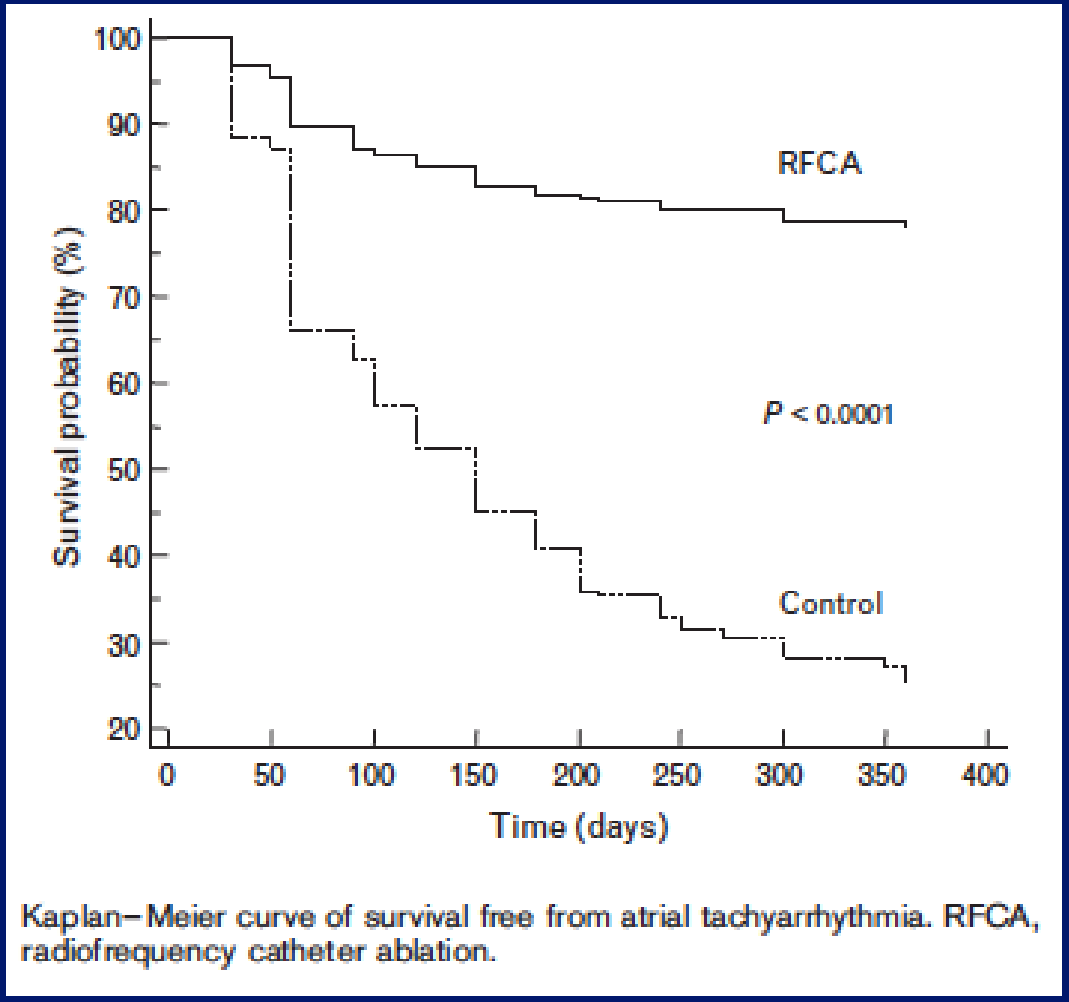


Moheri et al. Arch Intern Med. 2008;168:581-6.

Ablation vs Drugs for AF

A meta-analysis of ablation vs drugs

Bonano et al. J Cardiovasc Med 2010 (Epub)

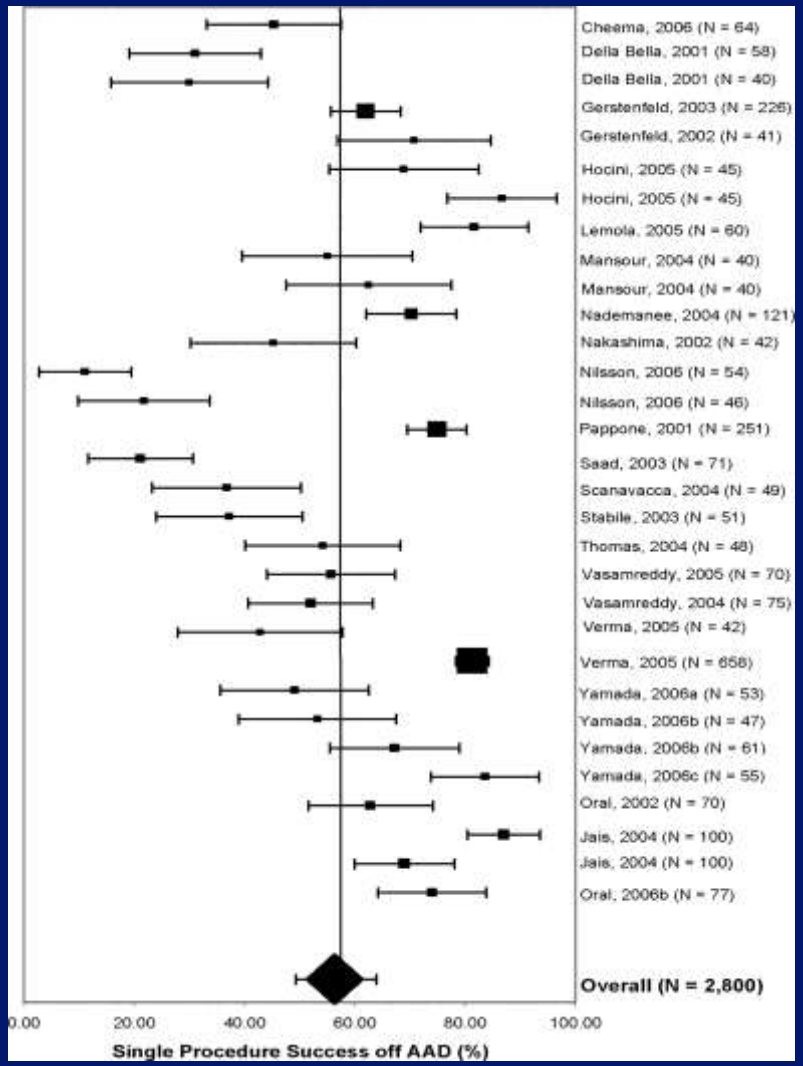


Kaplan–Meier curve of survival free from atrial tachyarrhythmia. RFCA, radiofrequency catheter ablation.

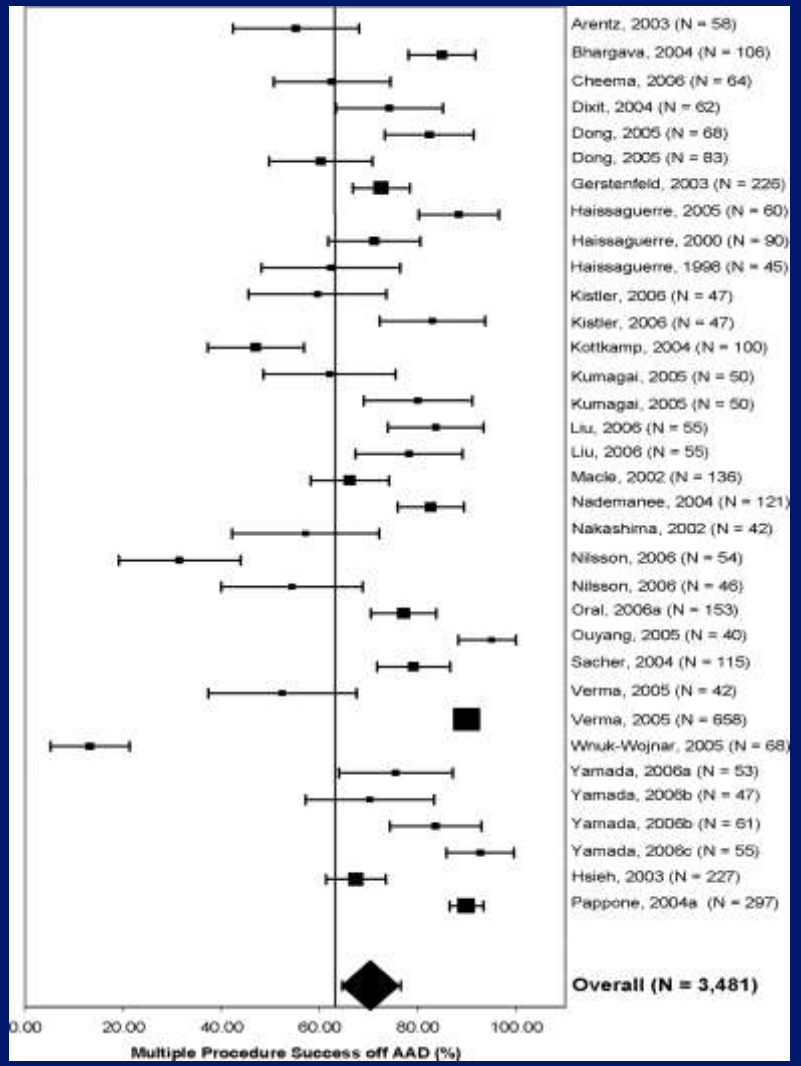
Ablation vs Drugs for AF

Efficacy of catheter ablations in AF

Calkins et al. Circ Arrhythmia Electrophysiol 2009;2:349-361



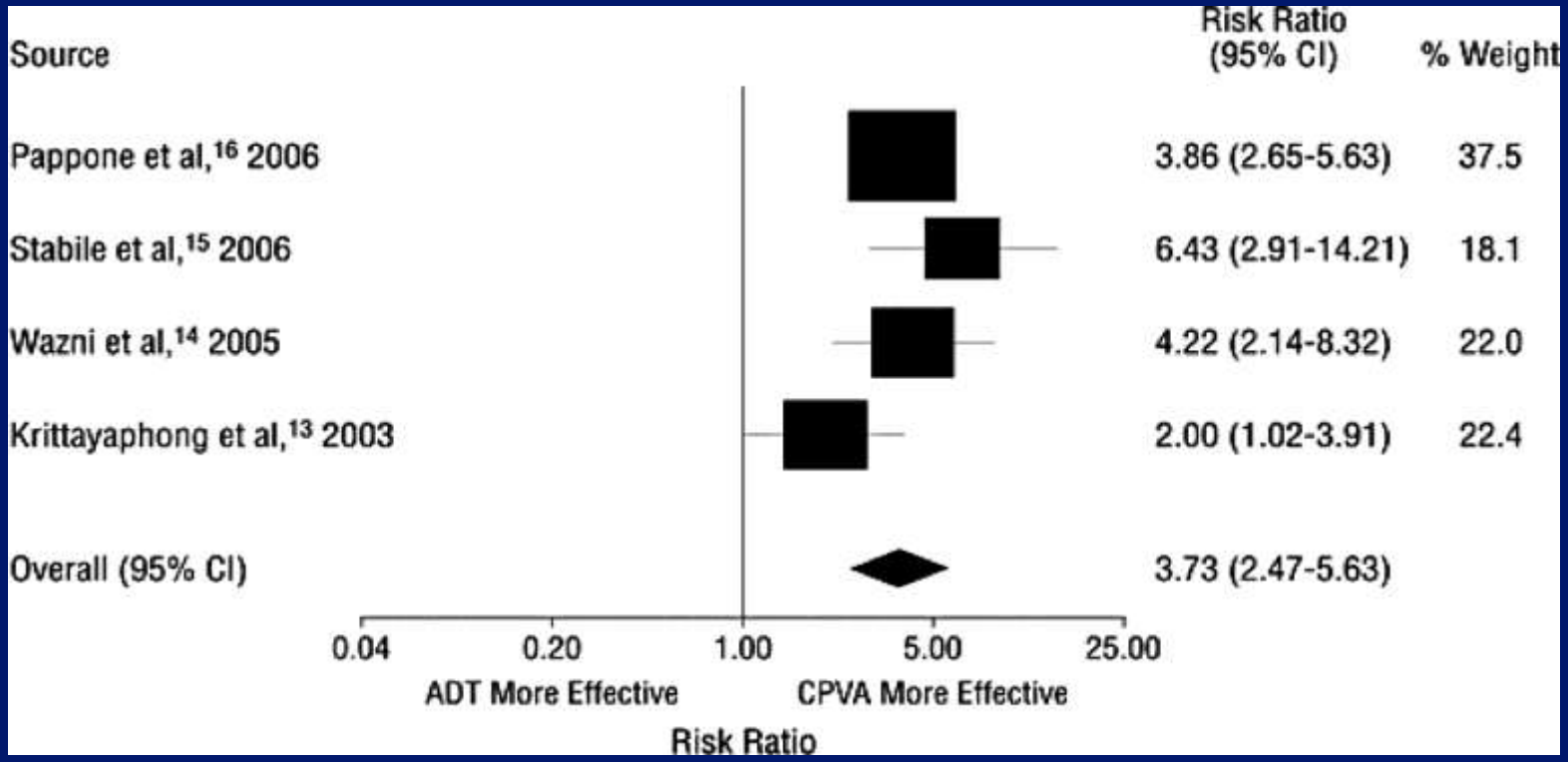
57% success rate



71% success rate

Ablation for AF

Catheter AblationTrials



Meta-analysis

Effect on arrhythmia recurrence

Noheria et al. Arch Intern Med 2008; 168:581

Ablation vs Drugs for AF

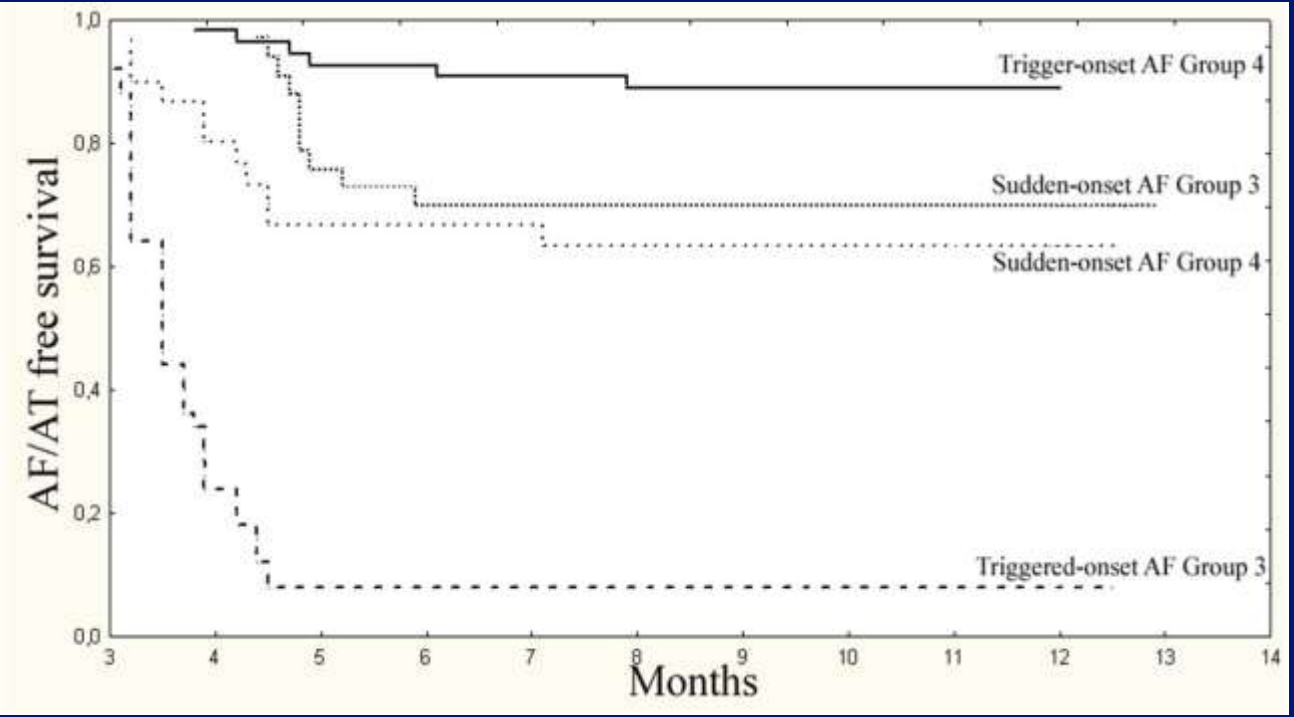
The Future

Forthcoming Ablation vs AAD Trials
Should Provide the Answer

RAAFT
CACAF-2
CABANA

Ablation for AF

Pokushalov et al. Circulation EP 2011 (E-Pub)
286 pts subjected to AF ablation and followed-up with Reveal XT

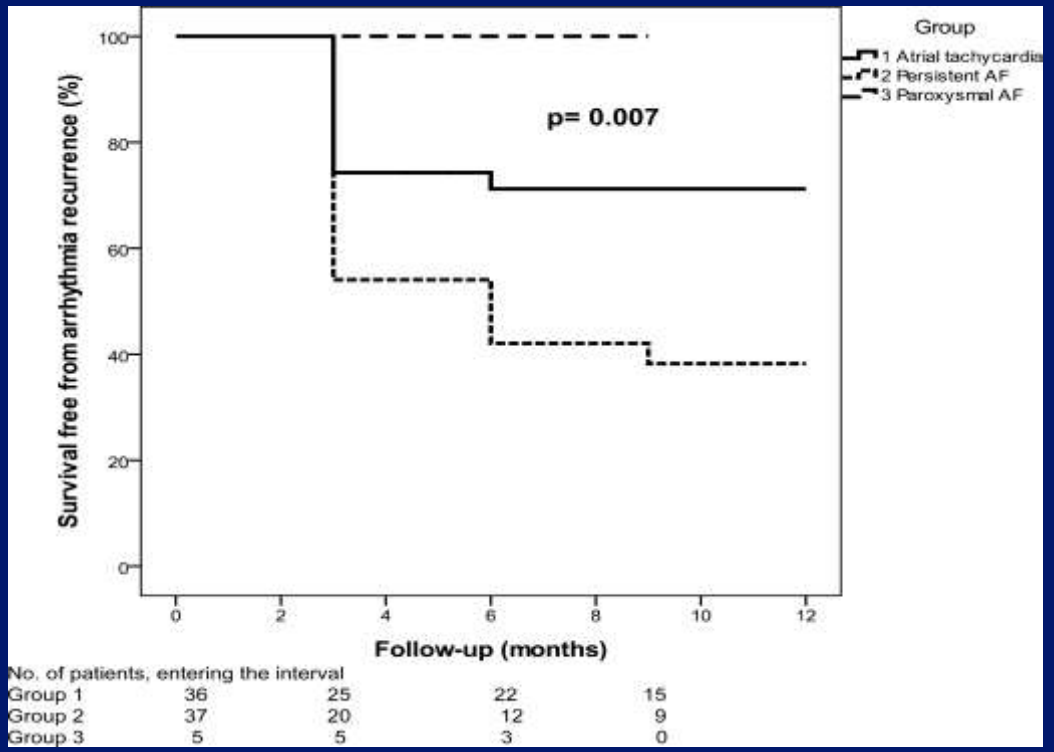


Trigger onset: AF triggered by AT/A Fl or APBs
Group 3: Re-ablation 3 months post-initial attempt
Group 4: Drugs or ablation depending on mode of onset

Ablation for AF

Ammar et al. Circulation EP 2011;4;609-614

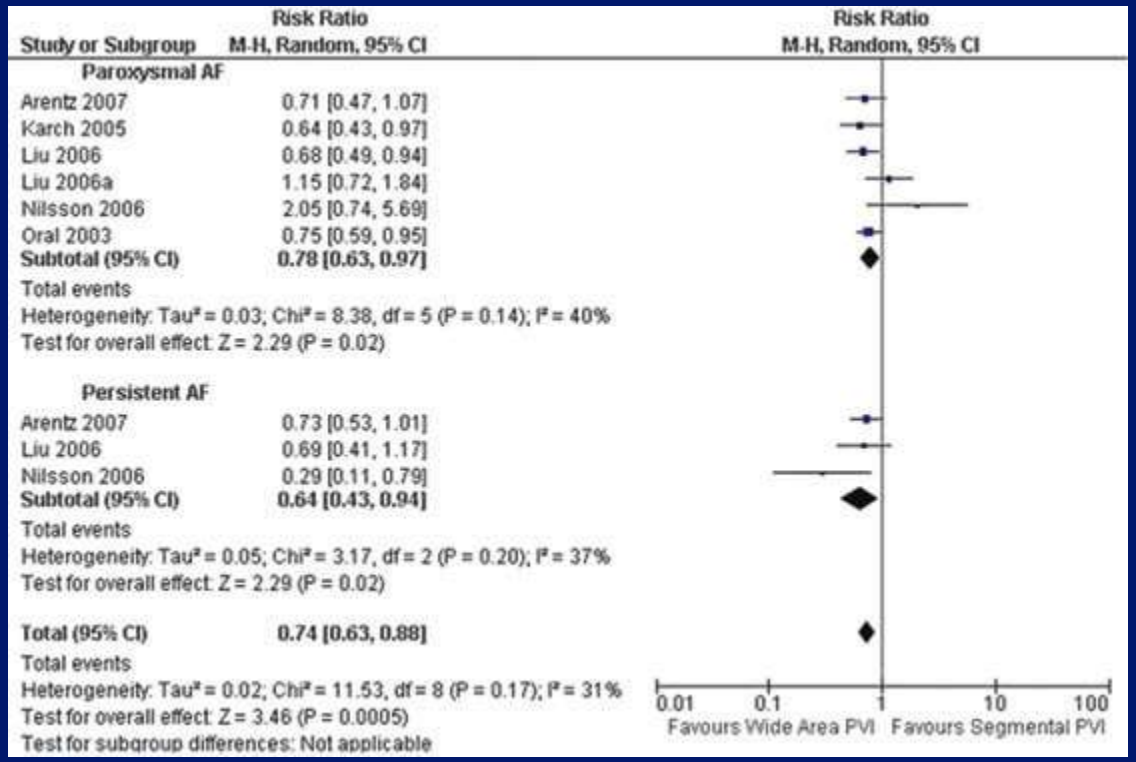
78 pts subjected to repeat ablation



Estimated probability of survival free from atrial arrhythmia recurrence after multiple repeat ablation procedures according to type of presenting arrhythmia for repeat ablation.

Ablation for AF

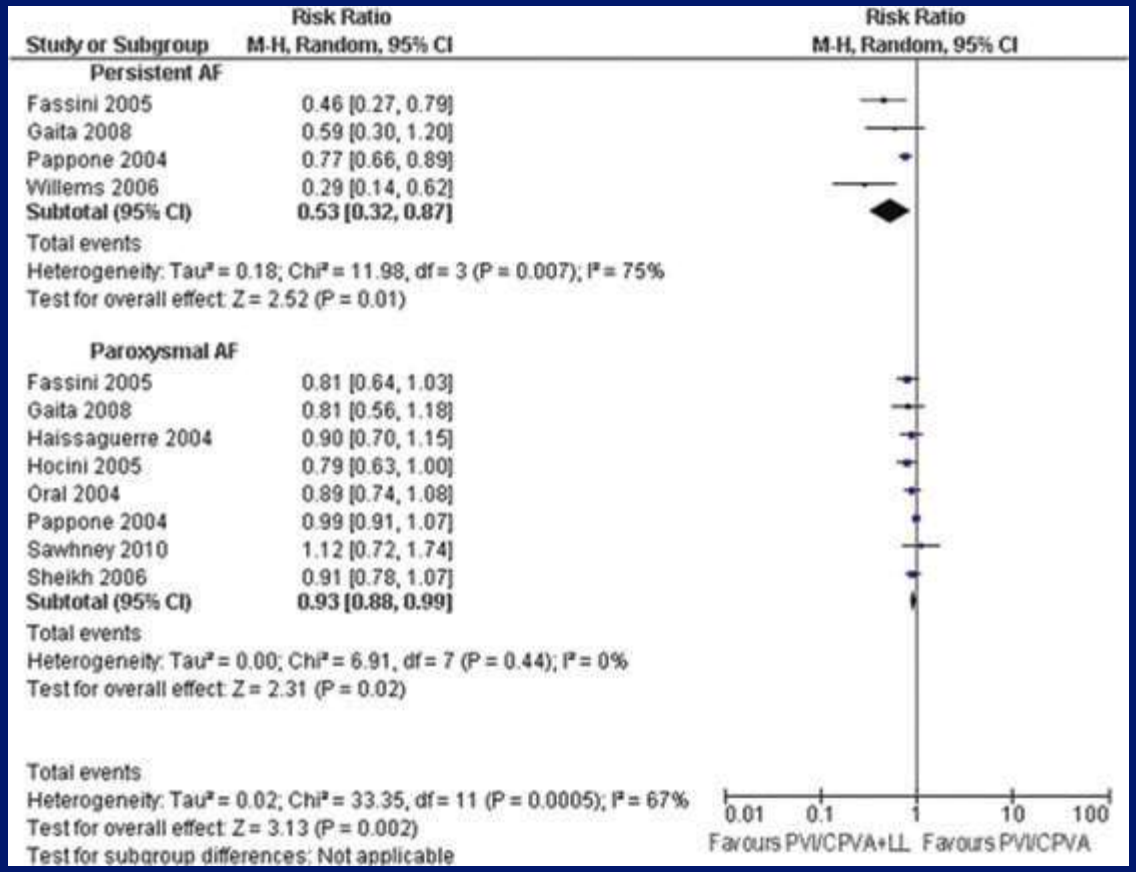
Parkash et al. A meta-analysis of RCTs. JCE 2001; 22:729-738



Segmental PVI versus wide area PVI: a random-effects model after a single procedure.

Ablation for AF

Parkash et al. A meta-analysis of RCTs. JCE 2001; 22:729-738

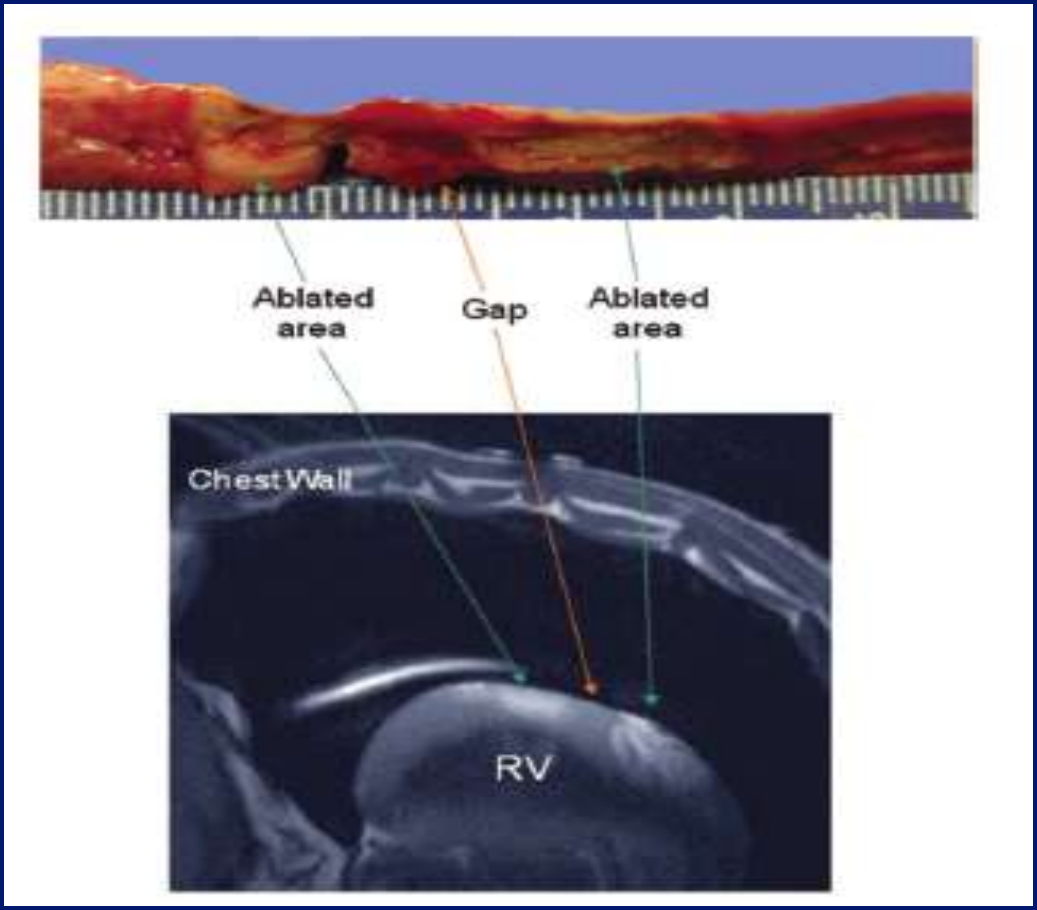


Addition of linear ablation to CPVA or PVI: a random-effects model after a single procedure.

Ablation for AF

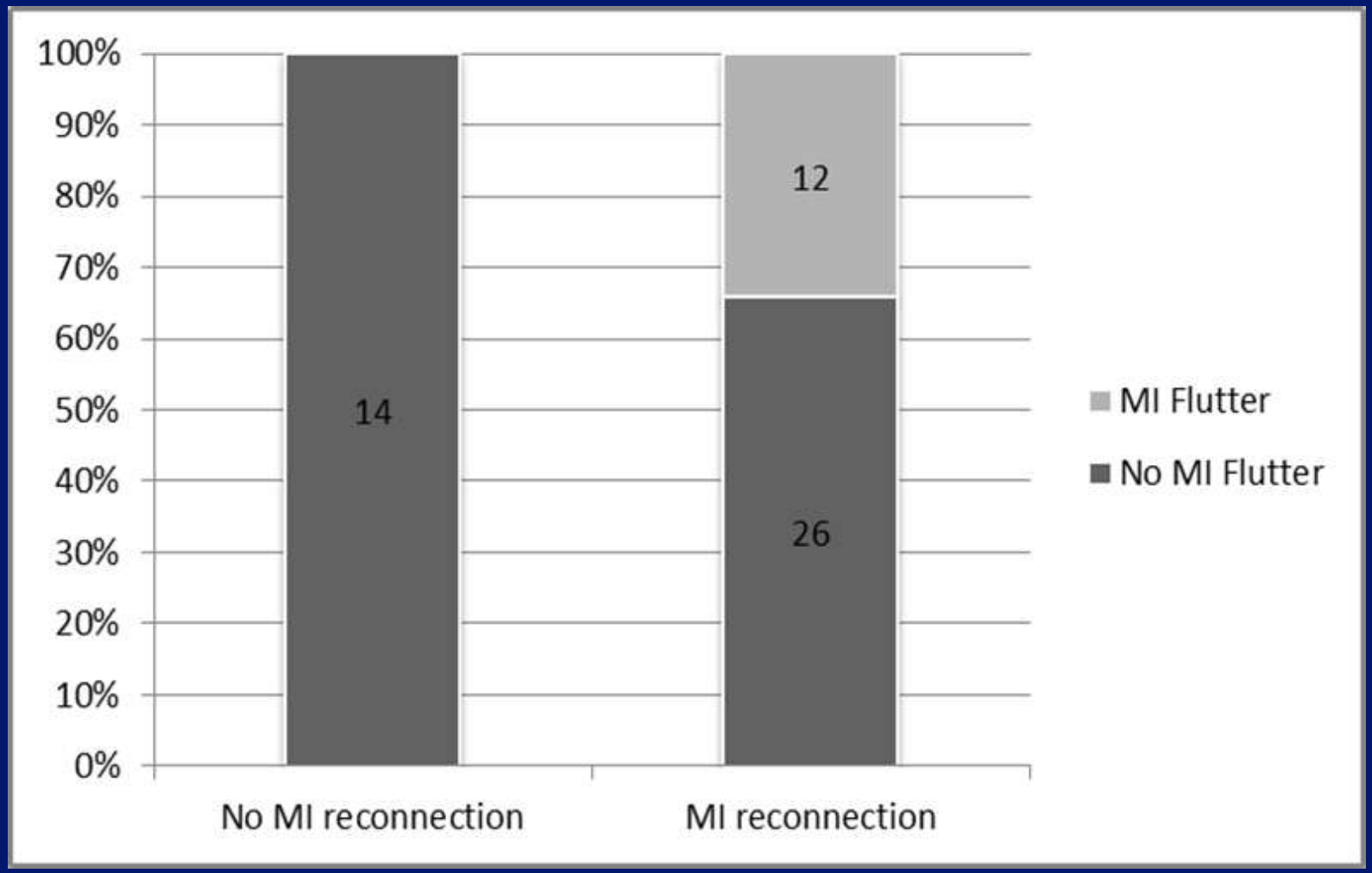
Gaps in the Ablation Line as a Potential Cause of Recovery From Electrical Isolation

Ranjan et al Circ Arrhythm Electrophysiol 2011;4;279-286



Ablation for AF

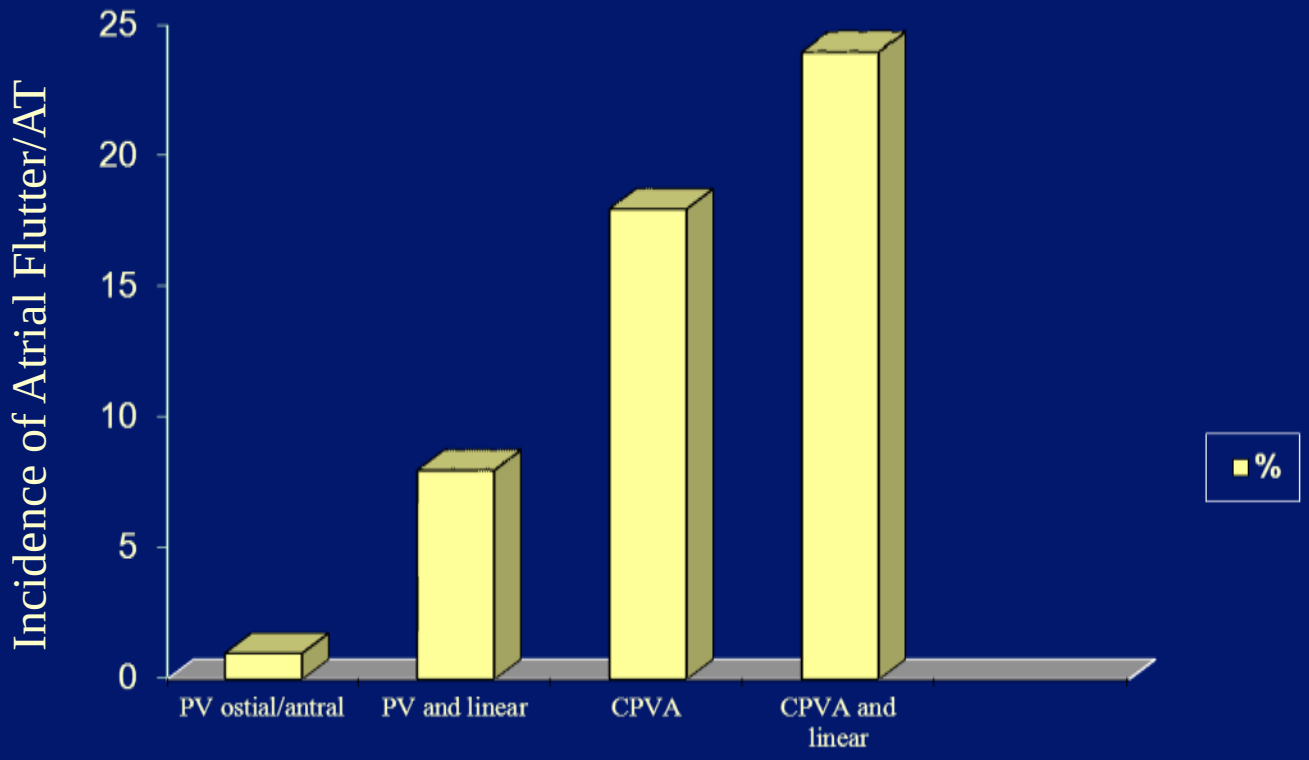
Recovery of Mitral Isthmus Conduction Leads to the Development of Macro-Reentrant Tachycardia after Left Atrial Linear Ablation for Atrial Fibrillation
Sawhney et al. Circulation AE (E-Pub)



Ablation for AF

Incidence of Ablation-Induced Tachycardias

544 patients Katritsis et al. JICE 2006;16:123

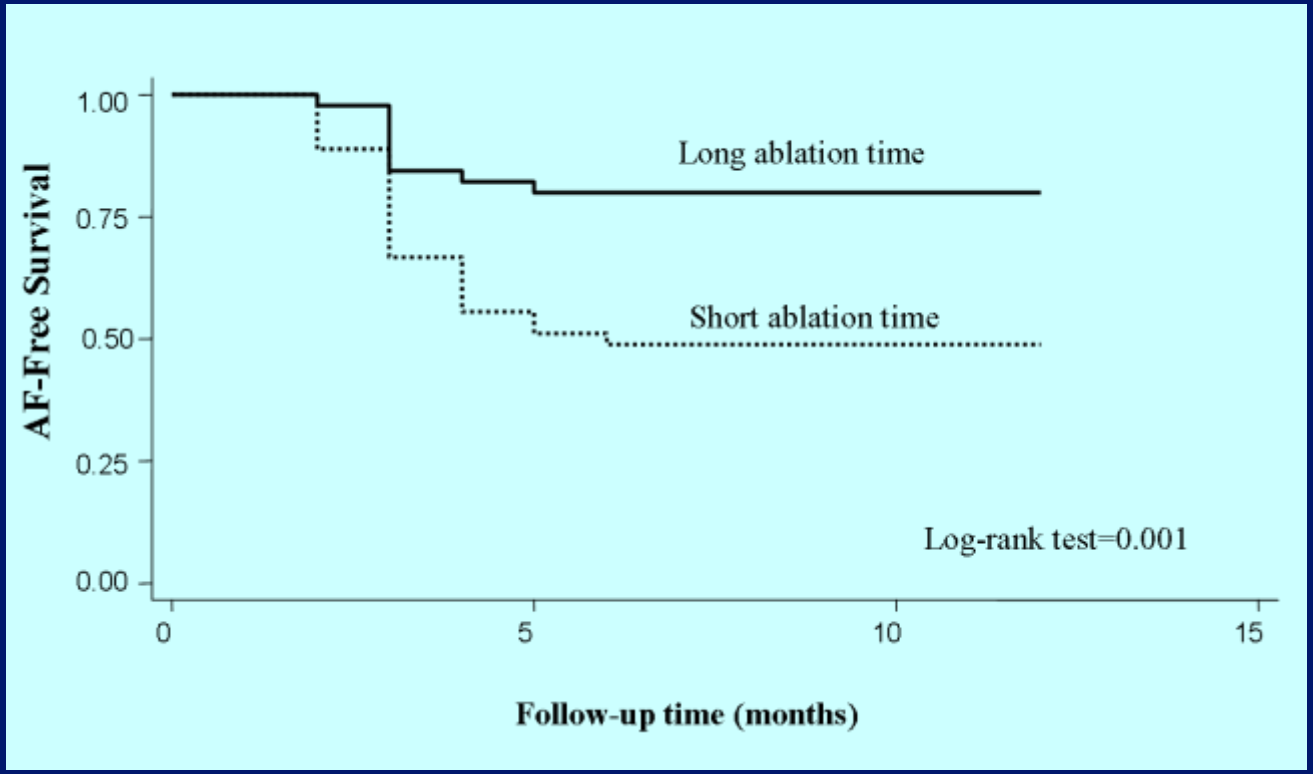


Ablation for AF

Extent of LA damage

Katritsis et al. JICE 2008;22:31-7

Radiofrequency Time is an independent predictor recurrence of AF 1 year after ostial (n=38) or circumferential (n=40) ablation.

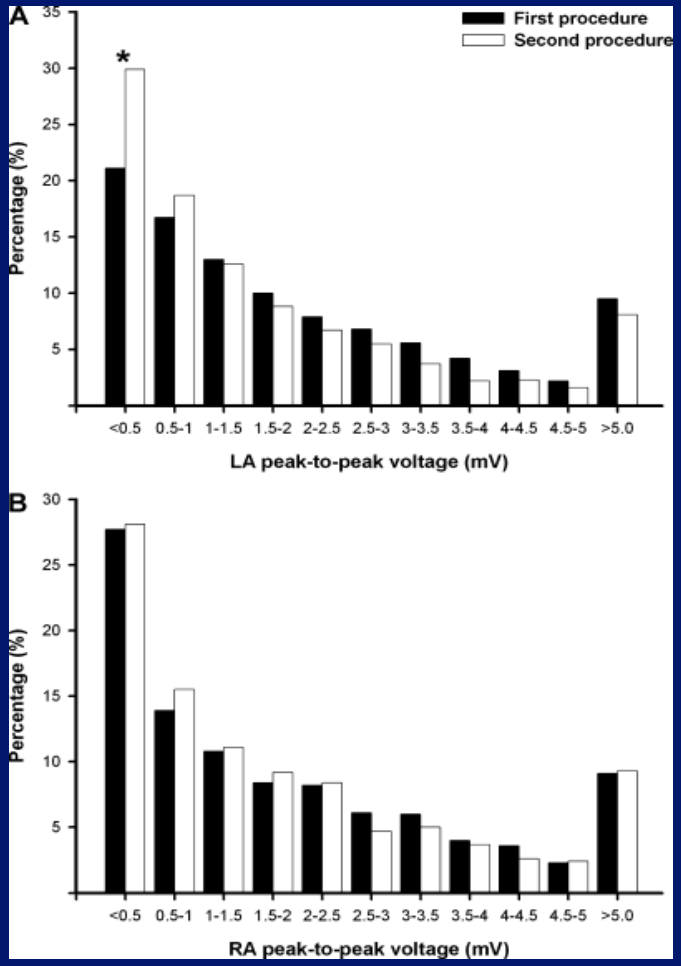


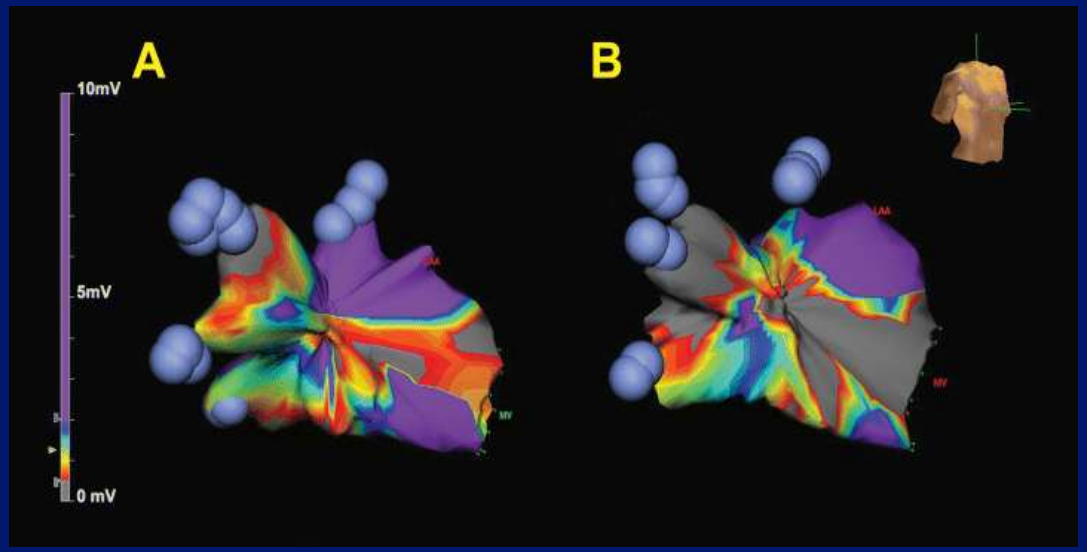
Ablation for AF

Extent of LA damage

Atrial substrate remodeling with a progressive decrease in the left atrial voltage was demonstrated in patients with recurrent AF

Lo et al. JCE 2007; 18: 258





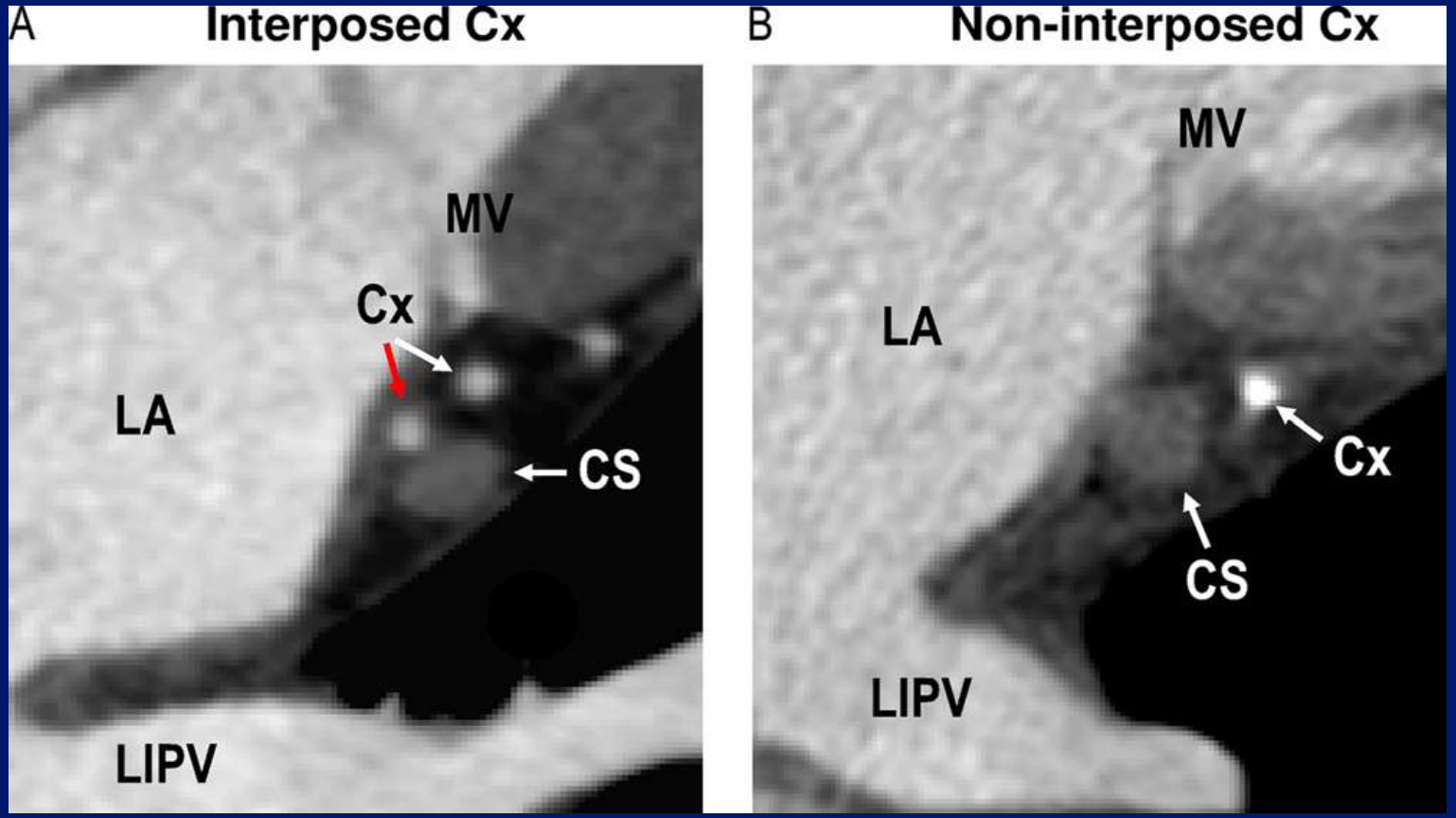
LA Fibrosis as AF Substrate

Kostin et al. Cardiovasc Res 2002; 54:361

Boldt et al. Heart 2004; 90:400

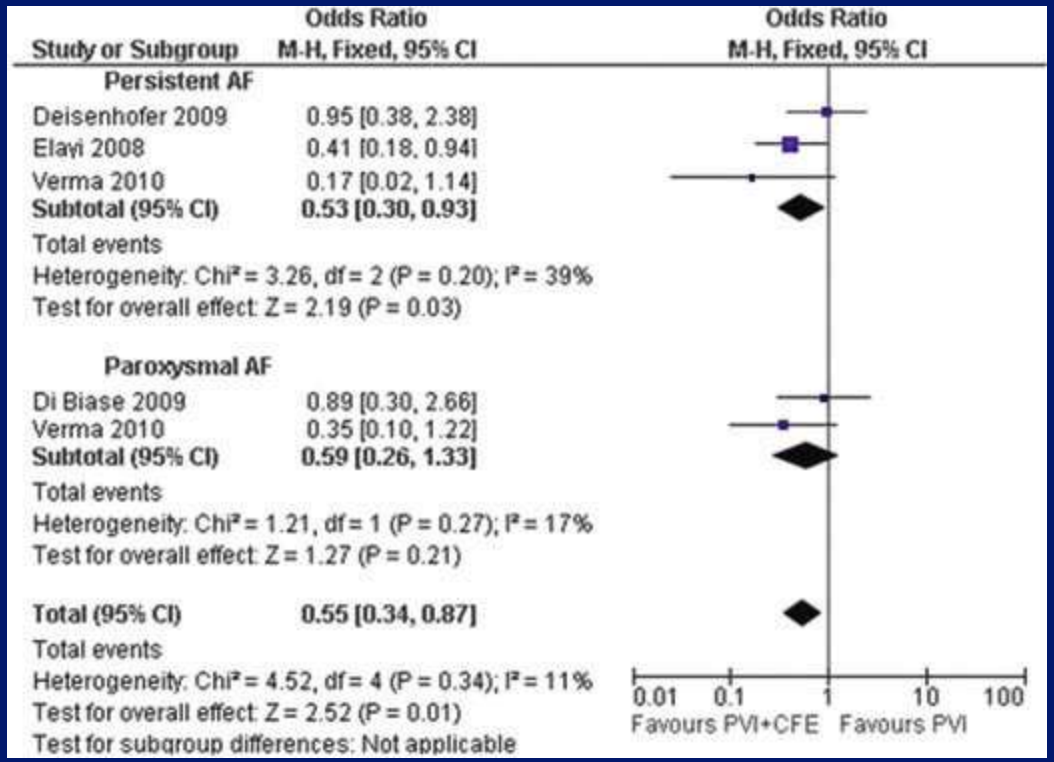
Ablation for AF

Interposition of the circumflex artery
between the mitral isthmus and the CS is associated with a lower probability of achieving complete mitral isthmus block.
Yokokawa et al. Heart Rhythm 2011;8:1404 –1410



Ablation for AF

Parkash et al. A meta-analysis of RCTs. JCE 2001; 22:729-738

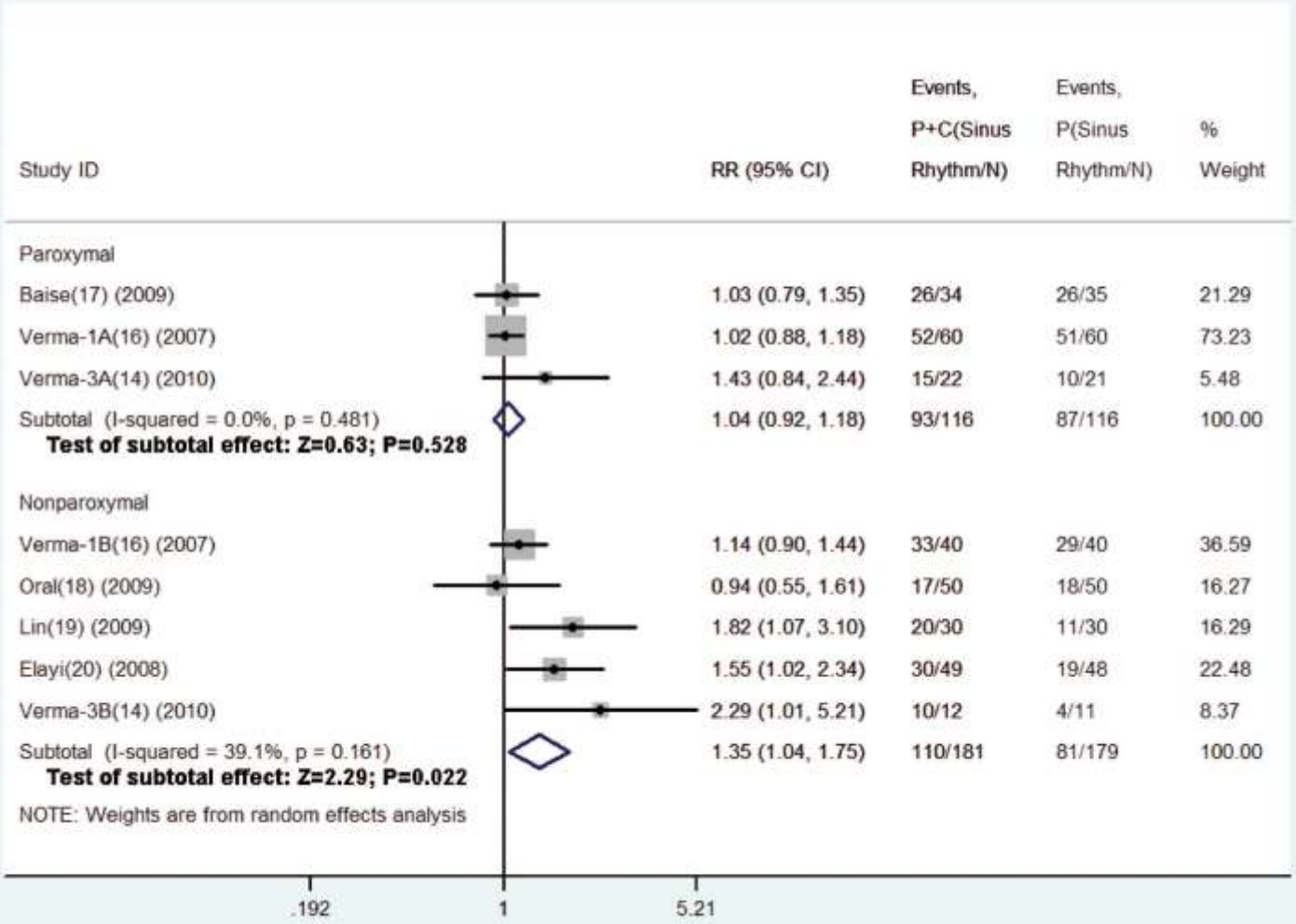


PVI versus PVI+CFE ablation:
a random-effects model after a single procedure.

Ablation for AF

PVI vs PVI + CFAE: a Meta-analysis

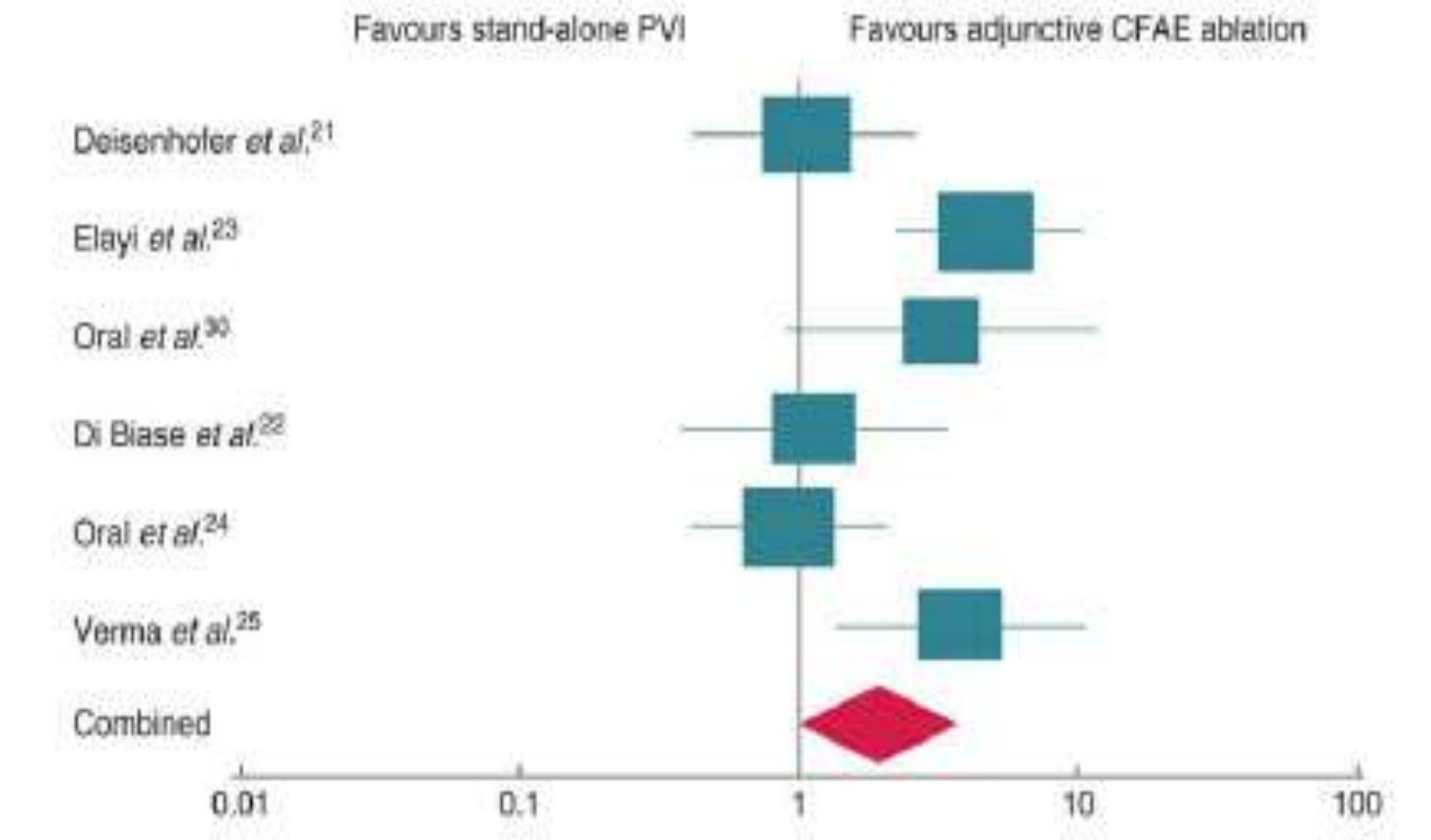
Li et al. Circ Arrhythm Electrophysiol. 2011;4:143-148



Ablation for AF

CFAE vs CFAE+PVI: a Meta-analysis

Kong et al. Europace 2011; 13: 193–204



Ablation for AF

CFAE vs CFAE+PVI: a Meta-analysis

Hayward et al. Heart Rhythm 2011;8:994 –1000

Study	PVI + CFAE n	PVI + CFAE N	PVI Alone n	PVI Alone N	Weight	Risk Ratio, 95% CI
Verma 2007	33	40	29	40	39.1%	1.14 [0.90, 1.44]
Elayi 2008	30	49	19	48	20.7%	1.55 [1.02, 2.34]
Lin 2009	21	30	12	30	15.9%	1.75 [1.06, 2.88]
Oral 2009	18	50	19	50	15.2%	0.95 [0.57, 1.58]
Verma 2010	10	12	5	11	9.1%	1.83 [0.91, 3.67]
Total (95% CI)		**181**		**179**	**100.0%**	**1.32 [1.05, 1.65]**
Total events	112		84			

Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 5.61$, $df = 4$ ($P = 0.23$); $I^2 = 29\%$

Test for overall effect: $Z = 2.41$ ($P = 0.02$)

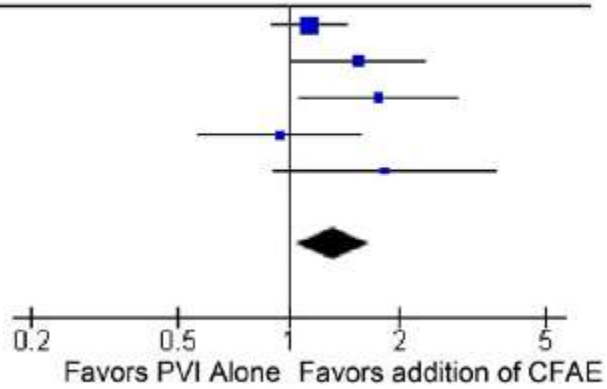
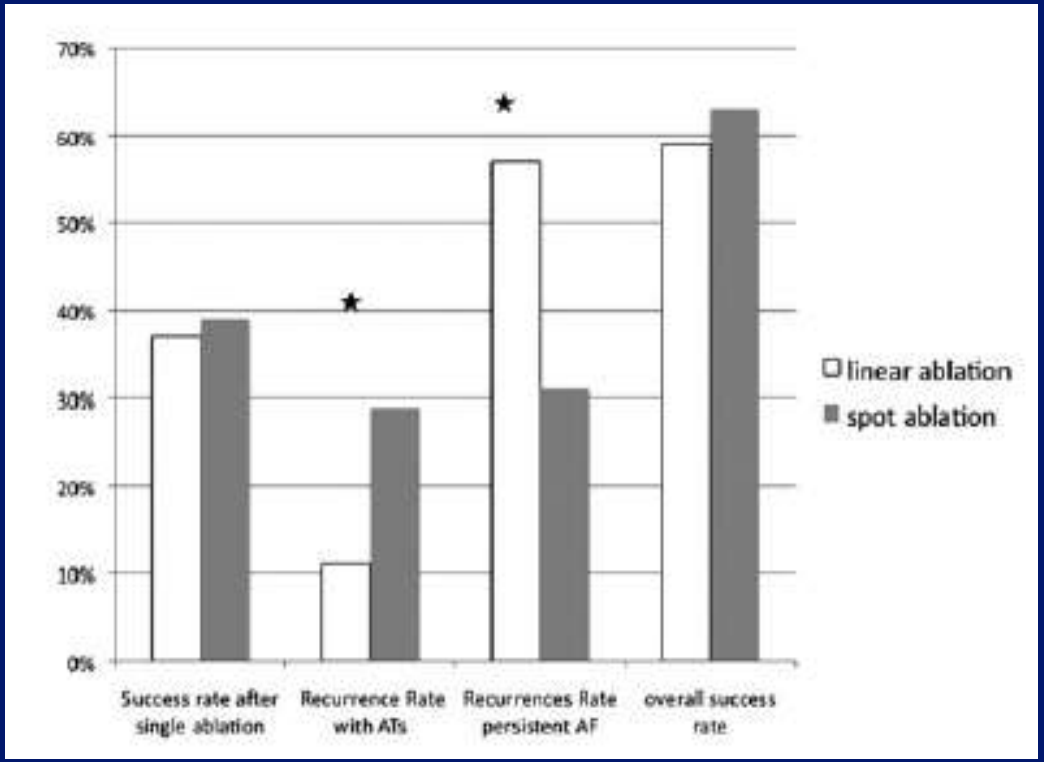


Figure 5 Freedom from atrial tachyarrhythmia for nonparoxysmal AF. AF = atrial fibrillation; CI = confidence interval.

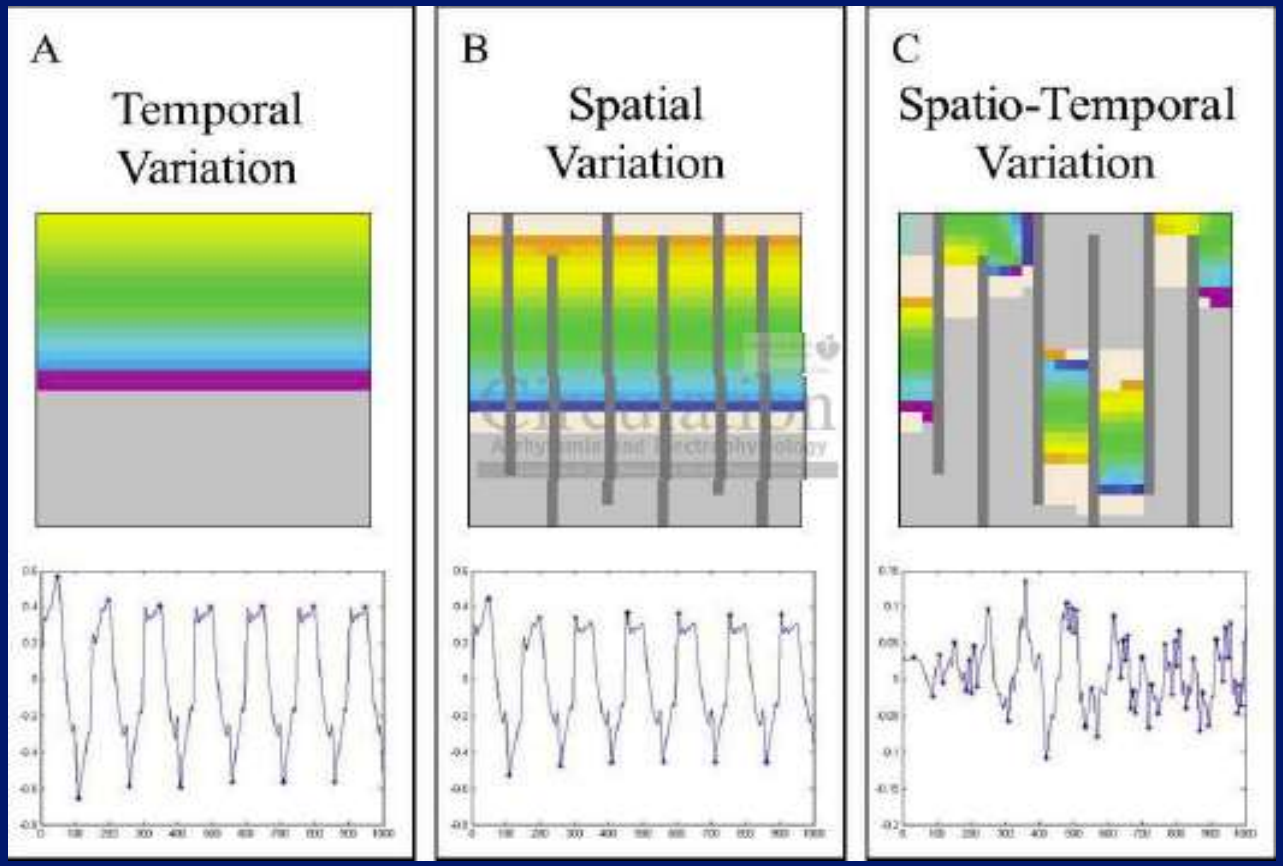
Ablation for AF

CFAE vs Linear Ablation in Persistennt AF: A Randomized Trial (116 pts)

Estner et al. *PACE 2011; 34:939–948*



Ablation for AF



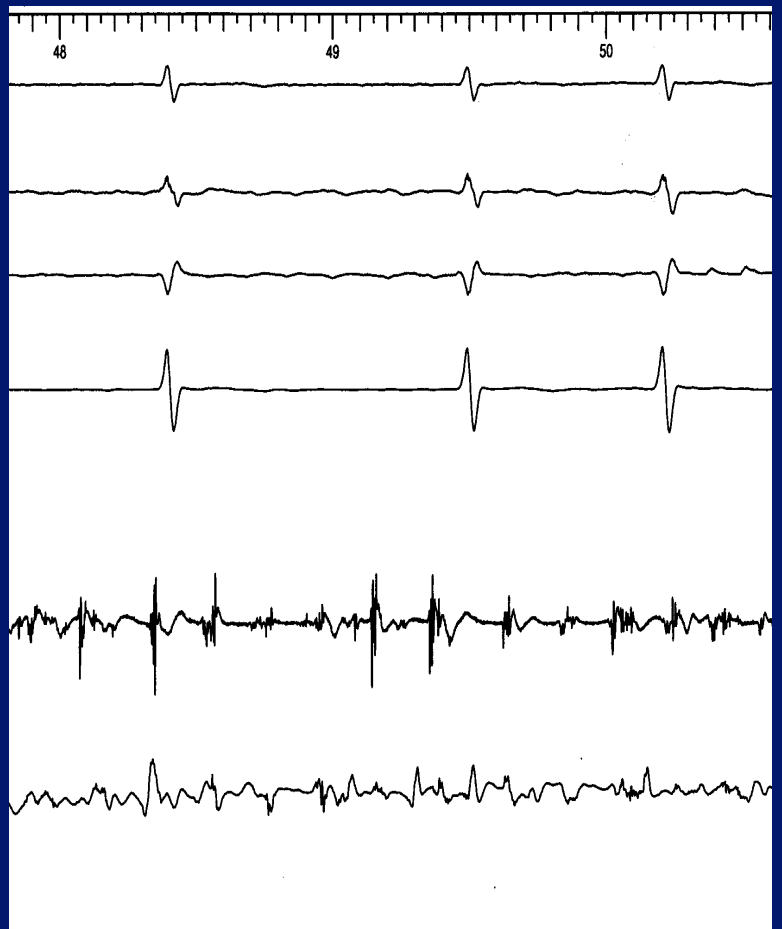
Corre a de Sa et al. Circulation AE 2011 (E Pub).

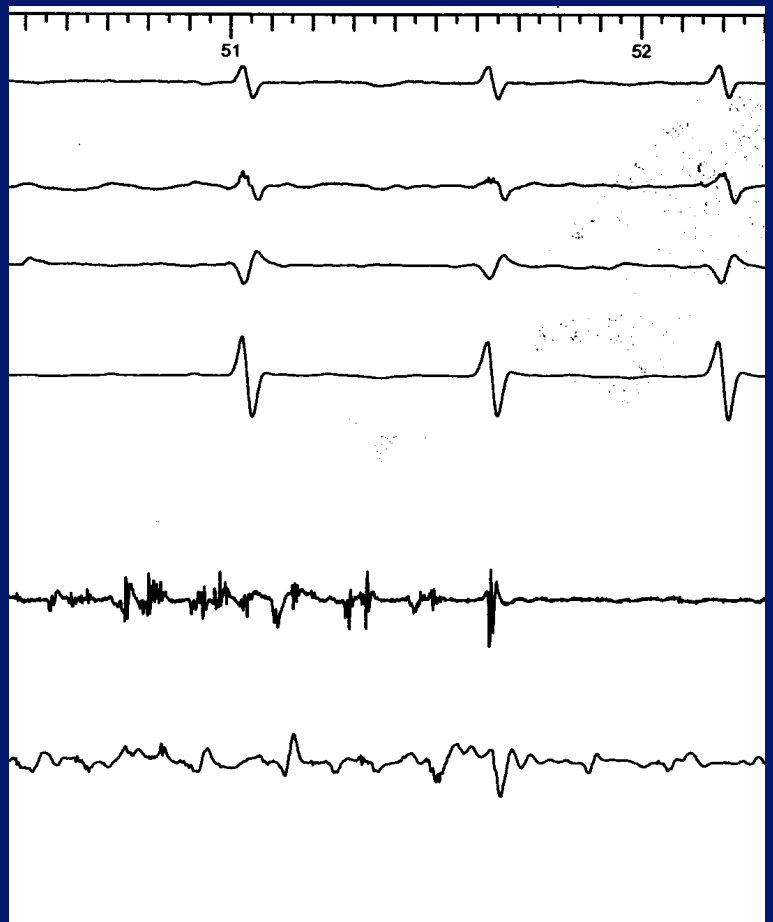
Ablation for AF

CFAEs and GP

Katritsis et al. Europace 2009;11:308-315

Complex Fractionated Atrial Electrograms at Anatomic Sites of Ganglionated Plexi in Atrial Fibrillation.

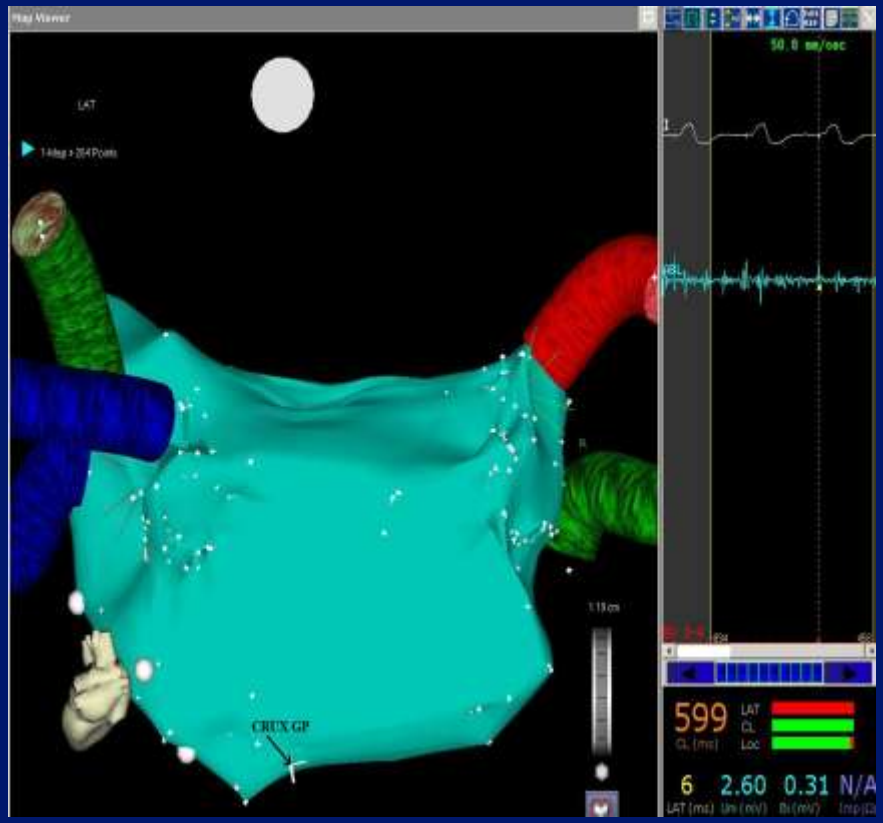


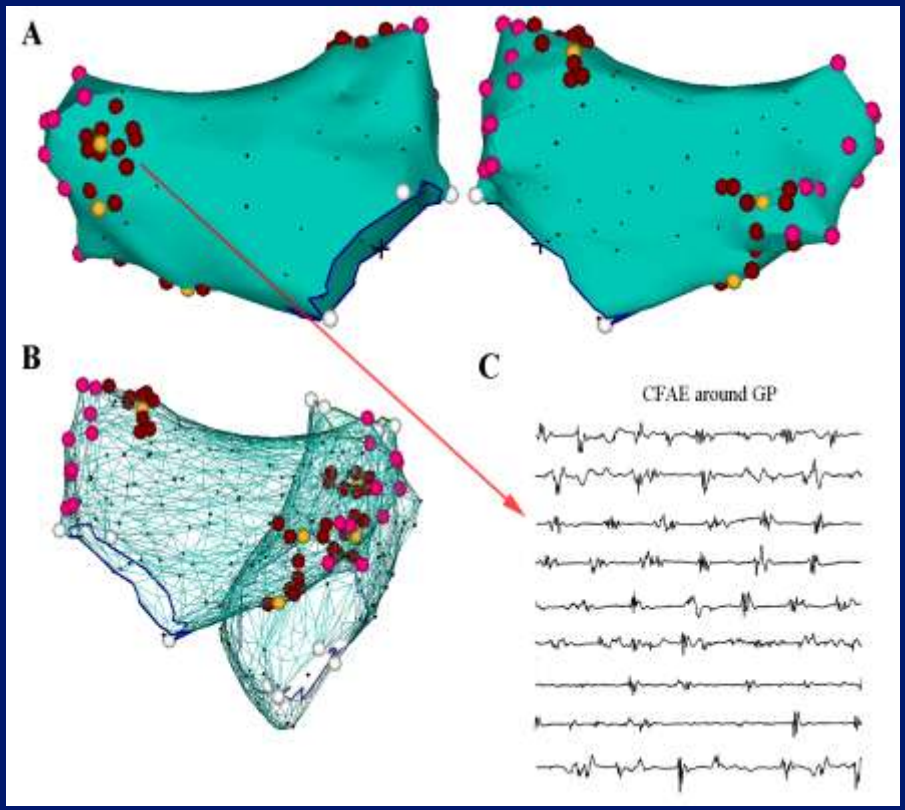


Ablation for AF

CFAEs at sites of GP

Katritsis et al. Europace 2009;11:308-315

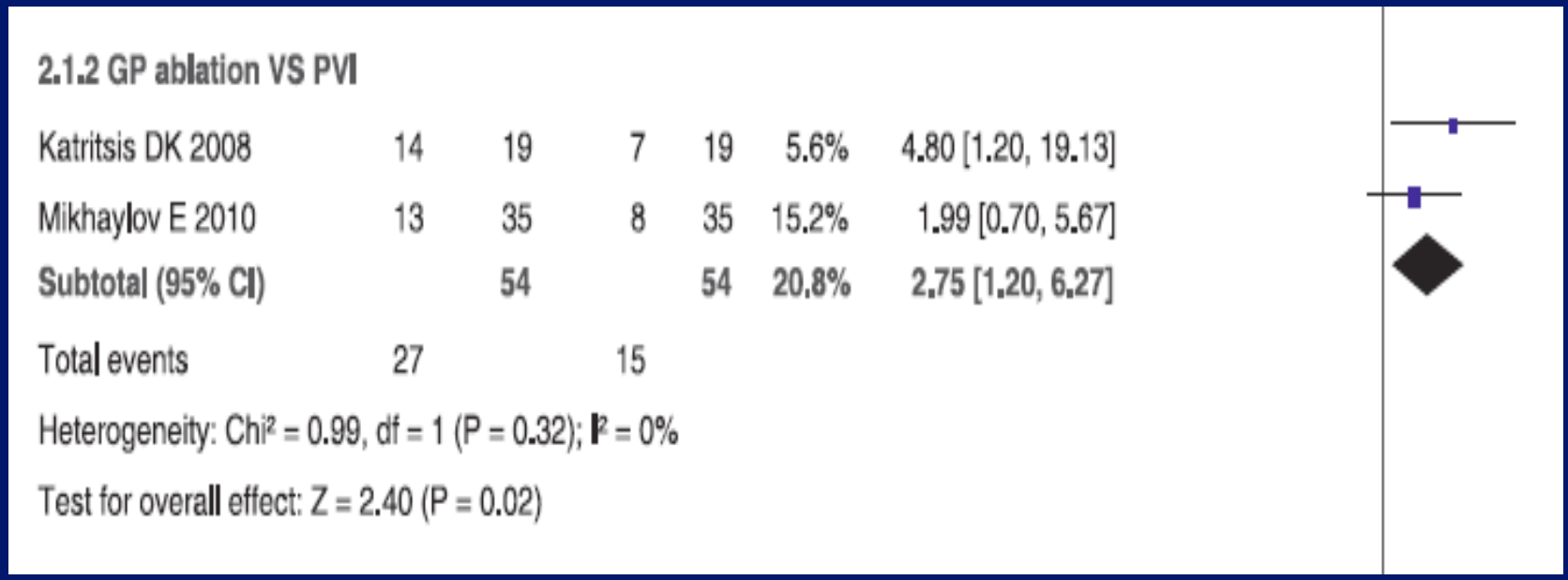




Ablation for AF

PVI vs GP: A meta-analysis

Zhou et al. PACE 2011; 1–8



2.1.2 GP ablation VS PVI						
Katritsis DK 2008	14	19	7	19	5.6%	4.80 [1.20, 19.13]
Mikhaylov E 2010	13	35	8	35	15.2%	1.99 [0.70, 5.67]
Subtotal (95% CI)		**54**		**54**	**20.8%**	**2.75 [1.20, 6.27]**
Total events	27		15			

Heterogeneity: $Chi^2 = 0.99$, df = 1 (P = 0.32); $I^2 = 0\%$

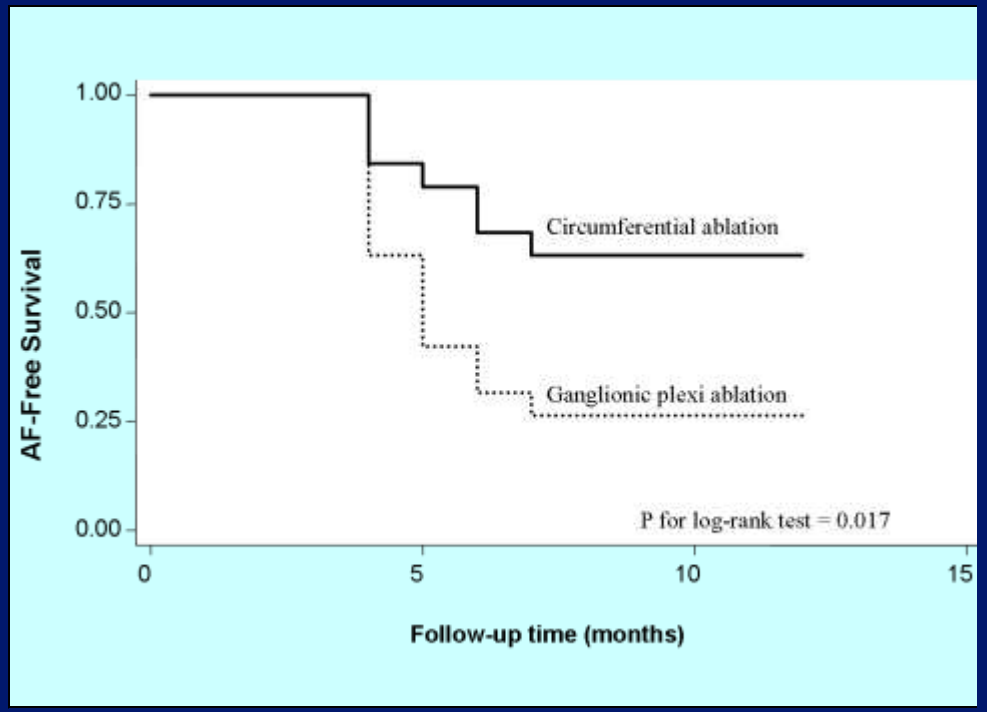
Test for overall effect: Z = 2.40 (P = 0.02)

Ablation for AF

Anatomic Ganglionic Plexi Ablation for Parasympathetic Denervation

Katritsis et al. Am J Cardiol 2008;102:330

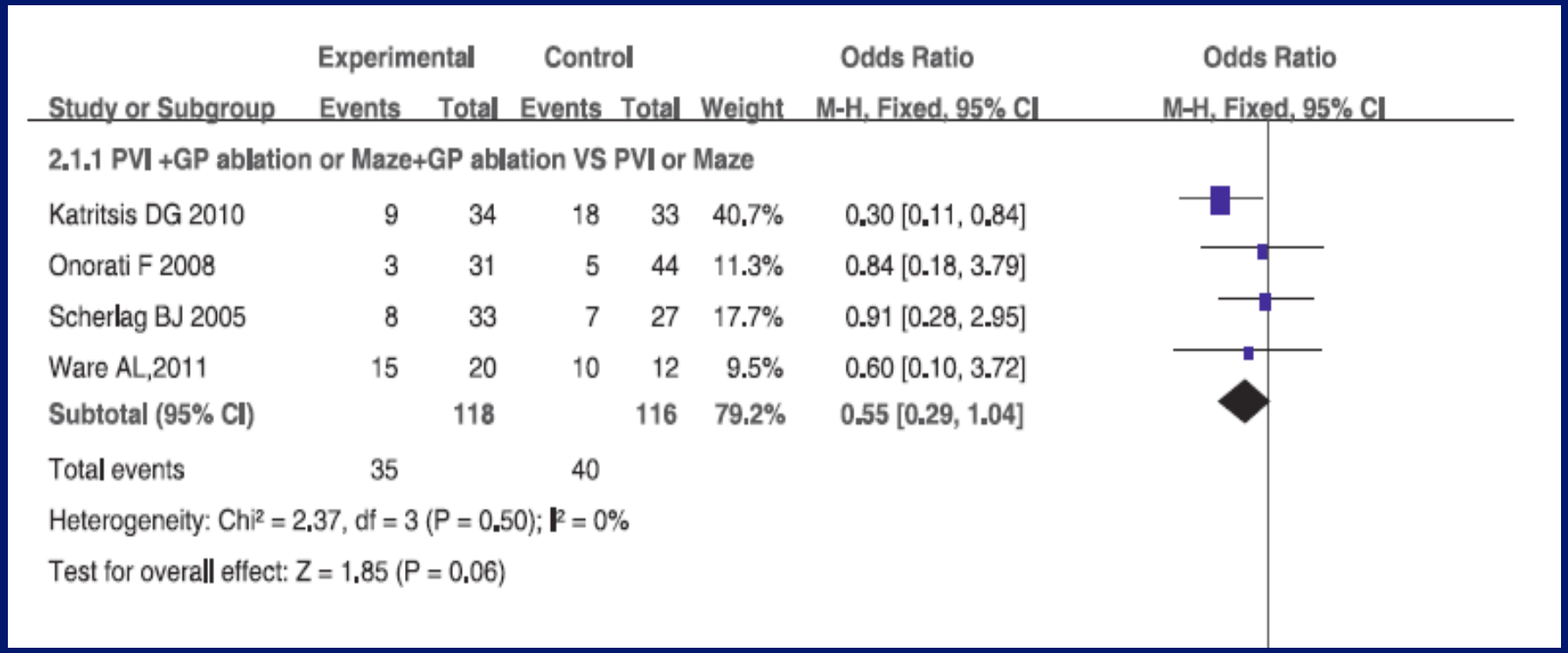
19 pts with CP anatomic ablation
compared to 19 age- and sex-matched controls
with circumferential ablation



Ablation for AF

PVI vs PVI+GP: A meta-analysis

Zhou et al. PACE 2011; 1–8



Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
2.1.1 PVI +GP ablation or Maze+GP ablation VS PVI or Maze						
Katritsis DG 2010	9	34	18	33	40.7%	0.30 [0.11, 0.84]
Onorati F 2008	3	31	5	44	11.3%	0.84 [0.18, 3.79]
Scherlag BJ 2005	8	33	7	27	17.7%	0.91 [0.28, 2.95]
Ware AL,2011	15	20	10	12	9.5%	0.60 [0.10, 3.72]
Subtotal (95% CI)		**118**		**116**	**79.2%**	**0.55 [0.29, 1.04]**
Total events	35		40			

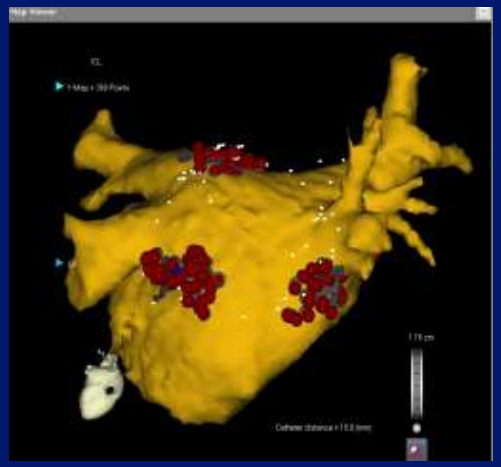
Heterogeneity: $Chi^2 = 2.37$, df = 3 (P = 0.50); $I^2 = 0\%$

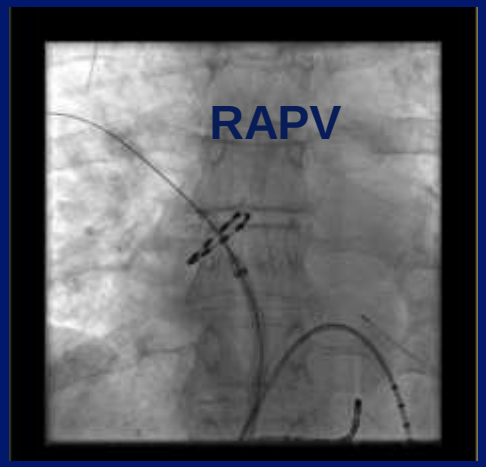
Test for overall effect: Z = 1.85 (P = 0.06)

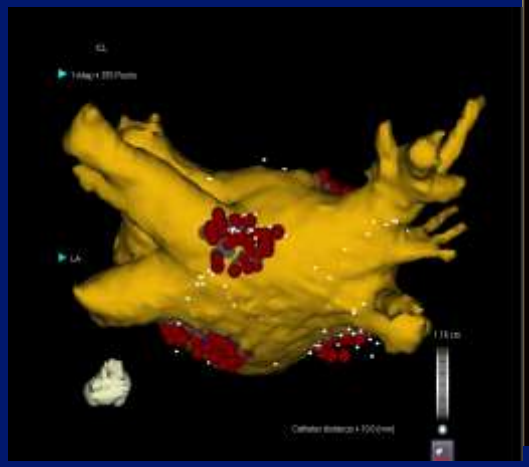
Odds Ratio M-H, Fixed, 95% CI

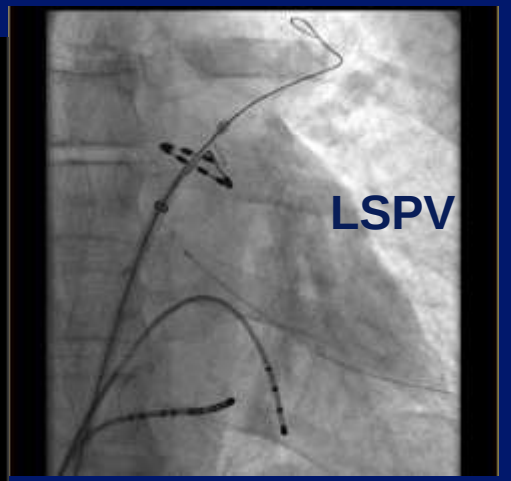
Ablation for AF

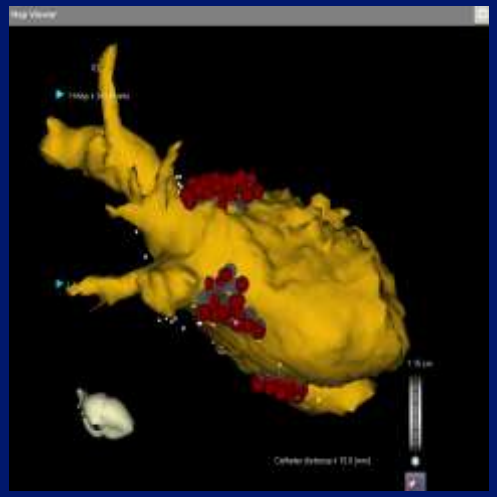
Athens Euroclinic: 78 pts > 60% 1-year success rate

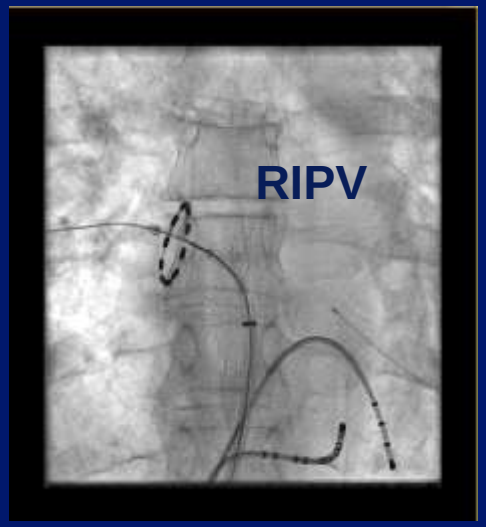


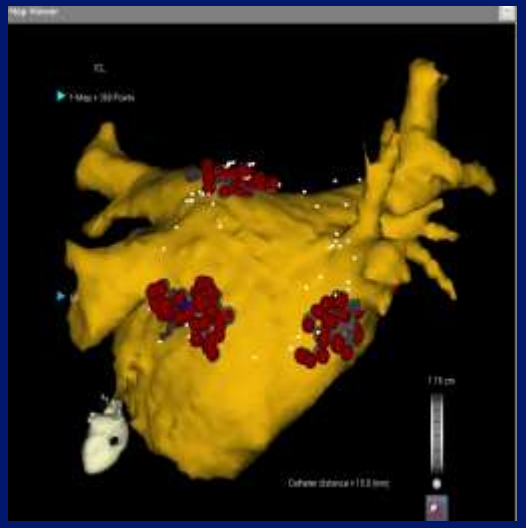


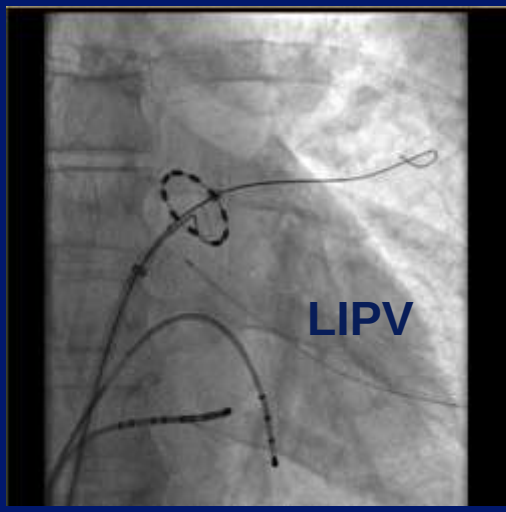








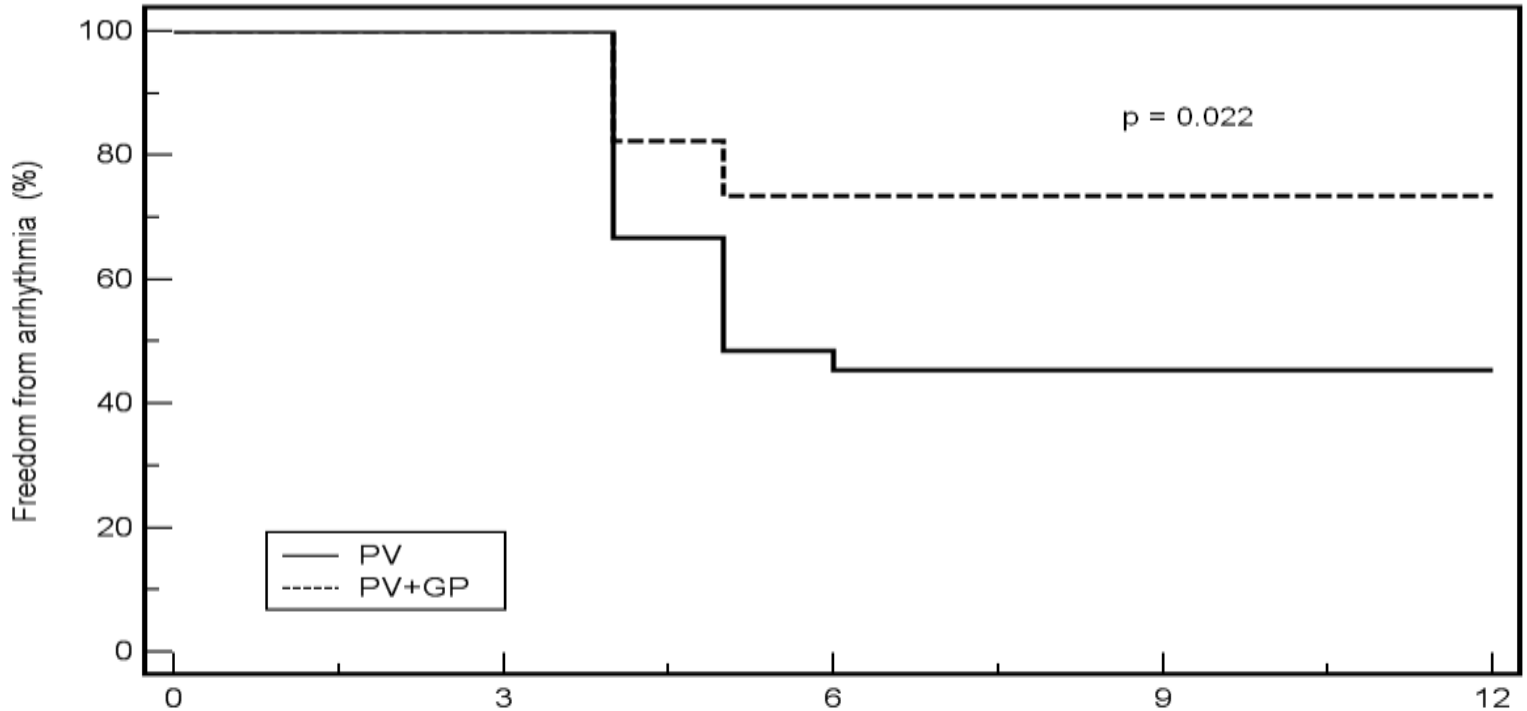




Ablation for AF

PV isolation (33 pts) vs PV isolation and anatomic GP ablation (34 pts)

Katritsis et al. HeartRhythm 2011;8:672-8



Number at risk

PV	33	33	15	15	15
PV+GP	34	34	25	25	25

Ablation for AF

Bohnen et al HeartRhythm 2011; 8:1661-1666

1676 pts (AF=784)

Major Complications of AF Procedures: 5.6%

Death: 0.1%
Perforation: 1.8%
Embolism: 1%
Aspiration pneumonia: 0.4%

Predictors of Complications:

Creatinine >1.5 mg/dl (P=0.3)

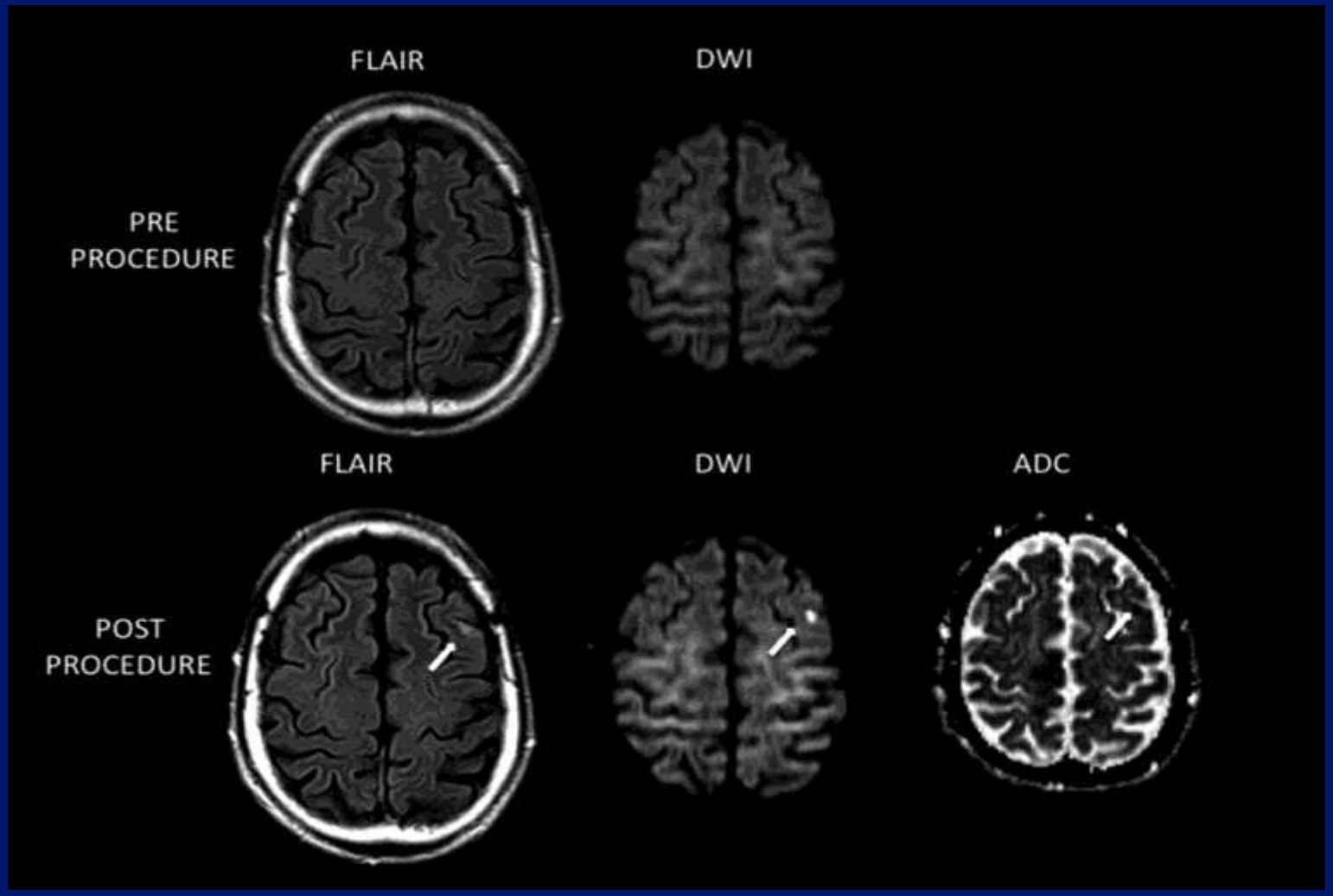
Prior CVA (P=0.8)

INR>2 (P=0.9)

Ablation for AF

232 pts: CVA 0.4%, MRI-detected embolism: 14%

Gaita, F. et al. Circulation 2010;122:1667-1673



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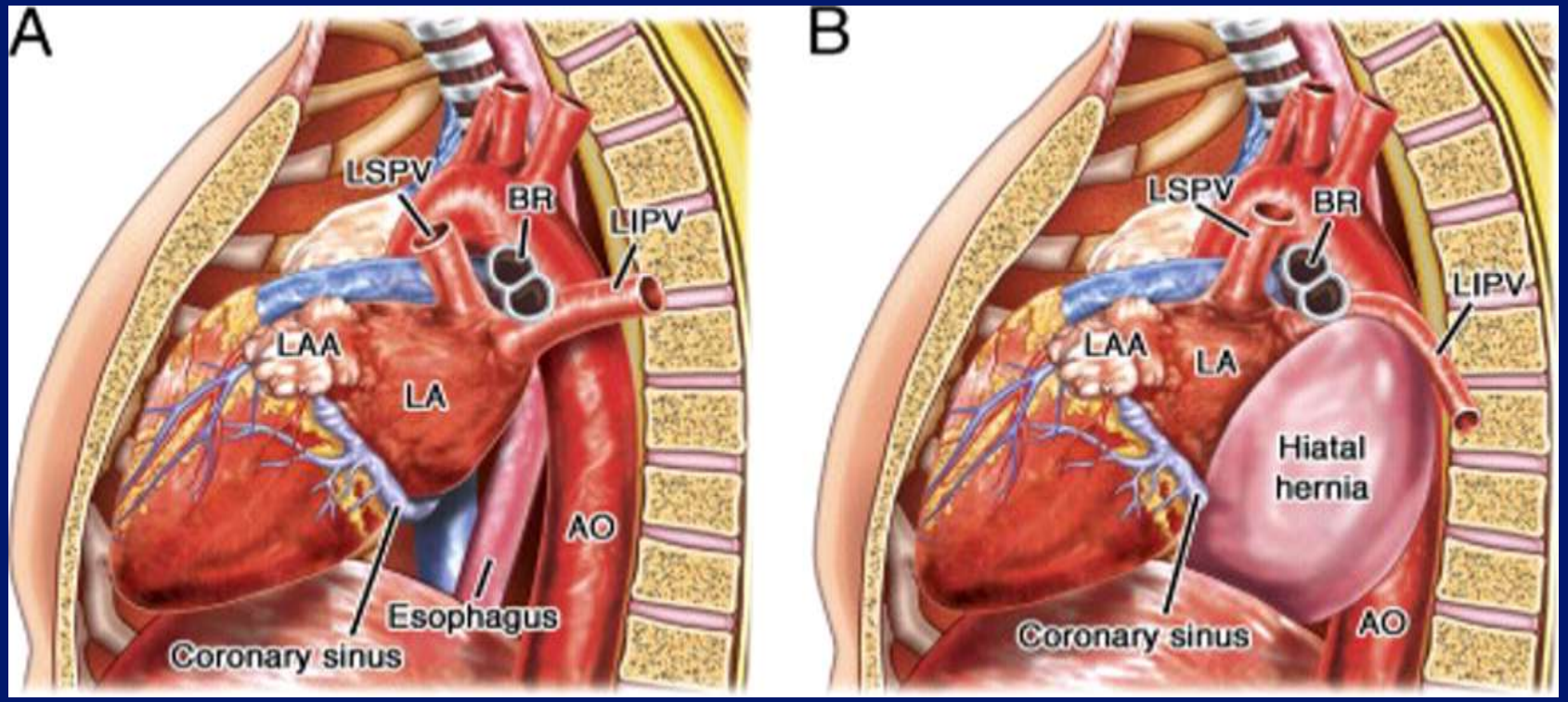
Up-stream Therapy

Cardiac and Esophageal Anatomical Relationship



Naoum, C. et al. J Am Coll Cardiol 2011;58:1624-1634

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Ablation for AF

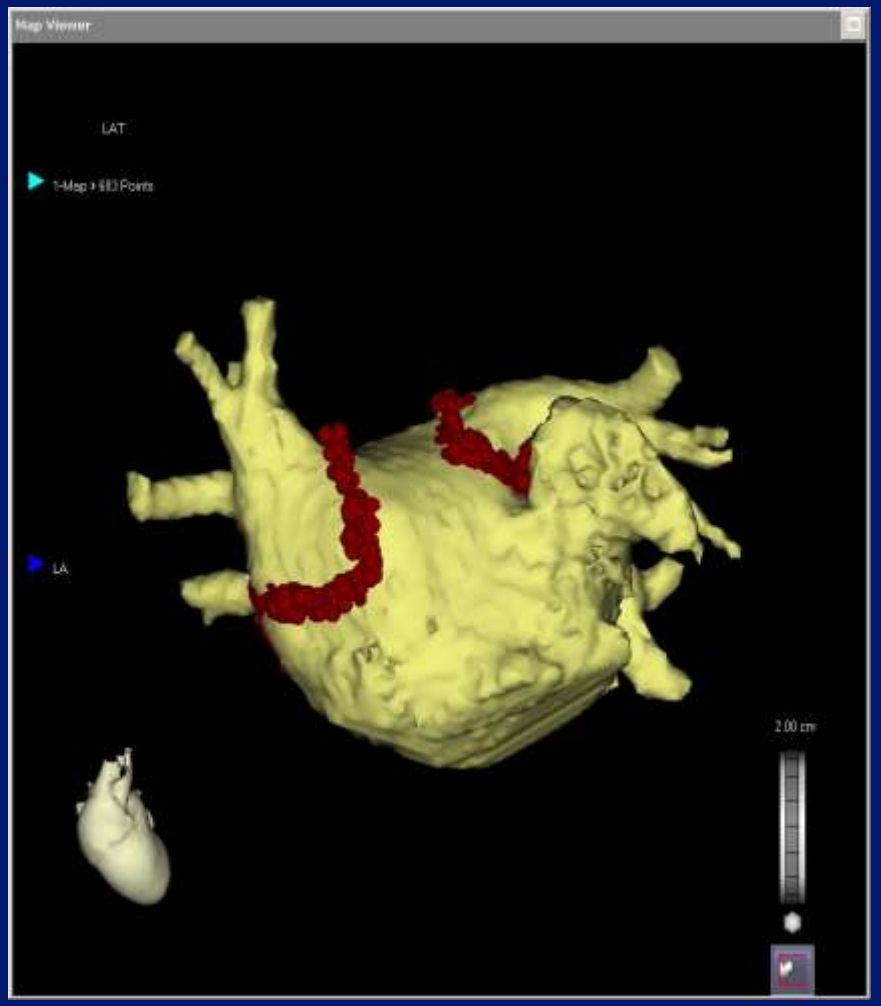
ΩΦΕΛΕΕΙΝ Η ΜΗ ΒΛΑΠΤΕΙΝ

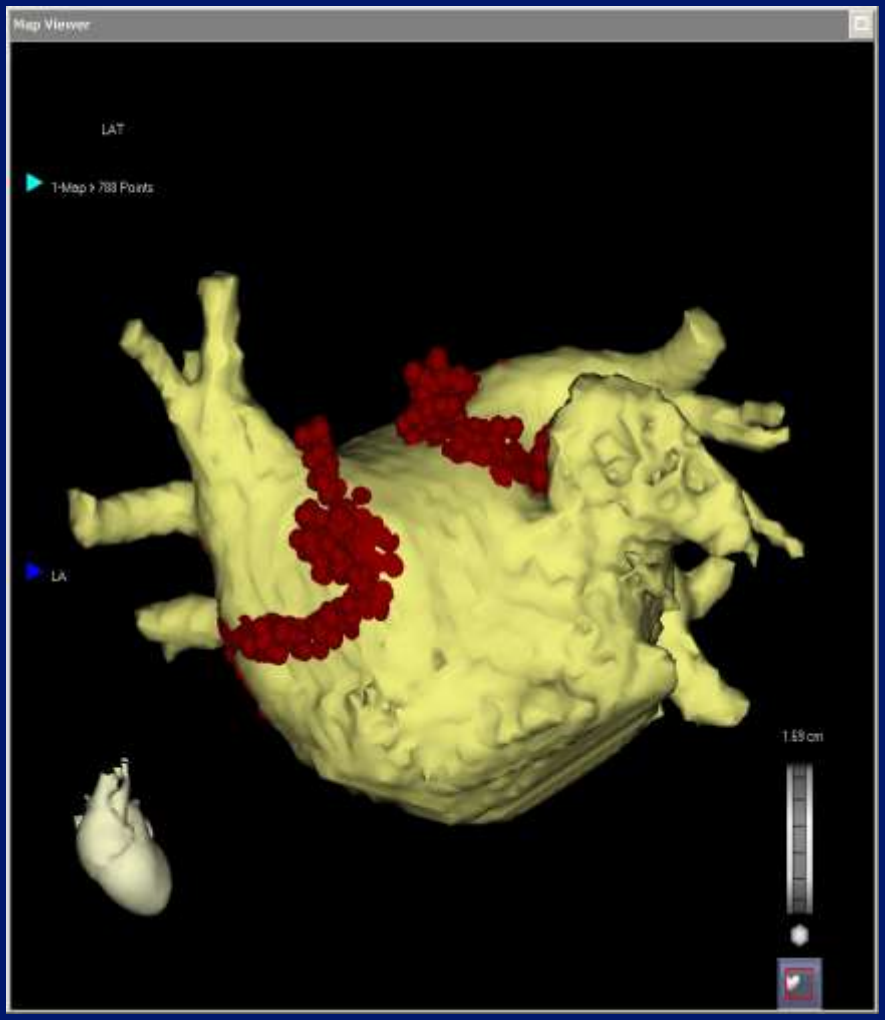
- 0.05% atrio-oesophageal fistulae?
  - Papone et al. Am J Cardiol. 2005;96:59L-64L.
- 1% atrio-oesophageal fistulae in surgical ablation
  - Doll et al. J Thorac Cardiovasc Surg. 2003;125:836
- 56% oesophageal ulcers in GP ablation (GA, 20-25 Watts)
  - Nakagawa HRS 2007

1. Avoid the posterior atrial wall
2. Administer PPIs for 14 days
3. Perform cardiac CT

(Martinek et al Heart Rhythm. 2010;7:1224-30: LA-Oesophagus >2 cm)

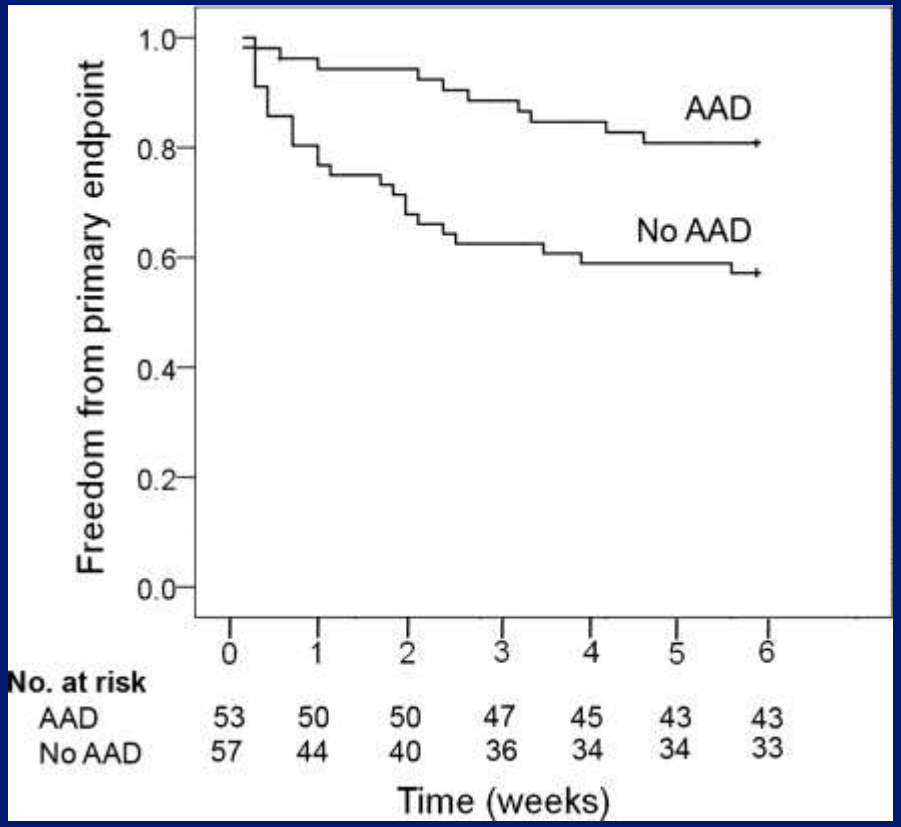
Ablation for AF



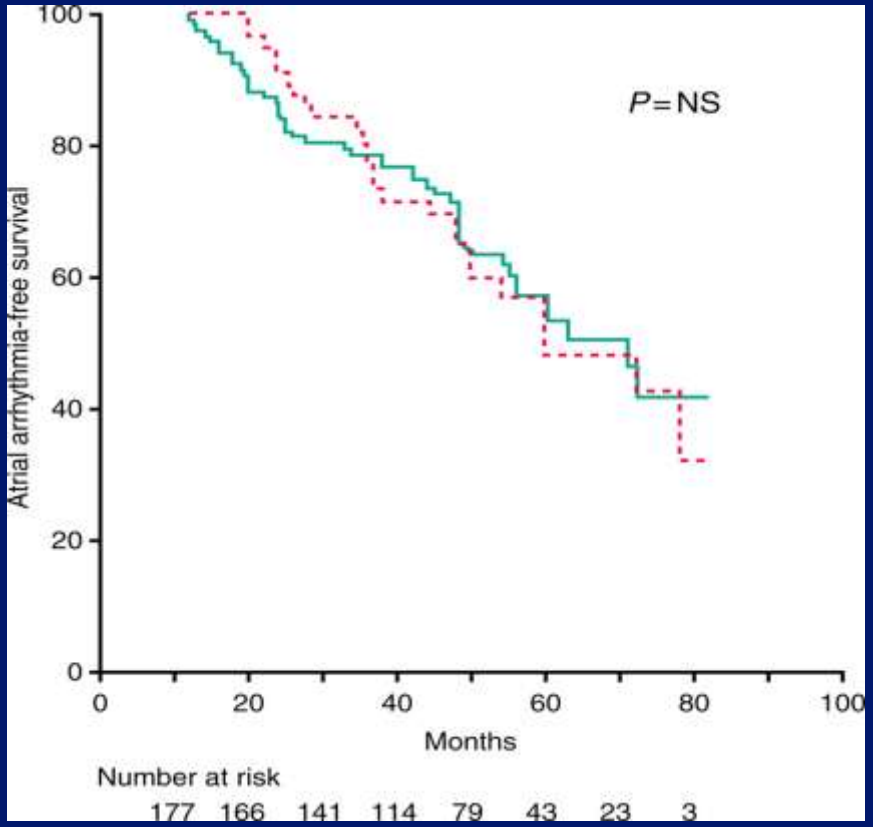


Ablation and Drugs for AF

Are Drugs and Ablation Needed ?



AADs 6 weeks post-ablation (5A)
110 pts
Roux et al. *Circulation 2009;120:1036-1040*



AADS 6 years post-ablation
229 pts (solid line pts on AADs)
Bertaglia et al. *Europace* 2009 0:eup349v1-349

Ablation for AF

Surgical Ablation

Conventional

Cox-MAZE III

Cox et al. A*nnals of Surgery*, 1996; 224:267-275.

Operative mortality 2%

Minimally Invasive

Robotic-assisted epicardial microwave

Pruitt et al. *Annals of Thoracic Surgery. 2006; 81: 1325-1331*

10% MAZE

Thoracoscopic PVI, GP ablation and appendage resection

Beyer et al. *Journal of Thoracic and Cardiovascular Surgery. 2009; 137:521-526*

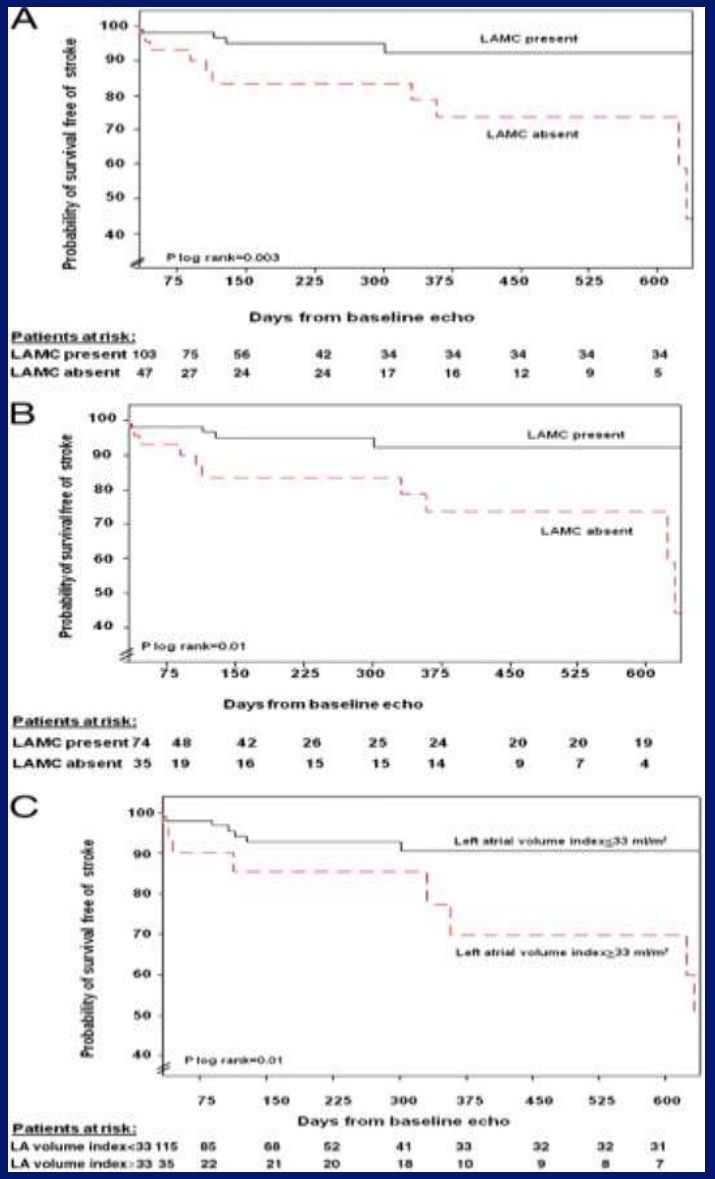
13% Complications

Surgery for AF

Stroke Event Rates

Absence of LA contraction and
LA volume index ≥33 ml/m^2
result in a significant increase in the risk
for thromboembolic stroke
after the Maze procedure
for patients in sinus rhythm

Buber, J. et al. J Am Coll Cardiol 2011;58:1614-1621



Surgery for AF

ESC 2010

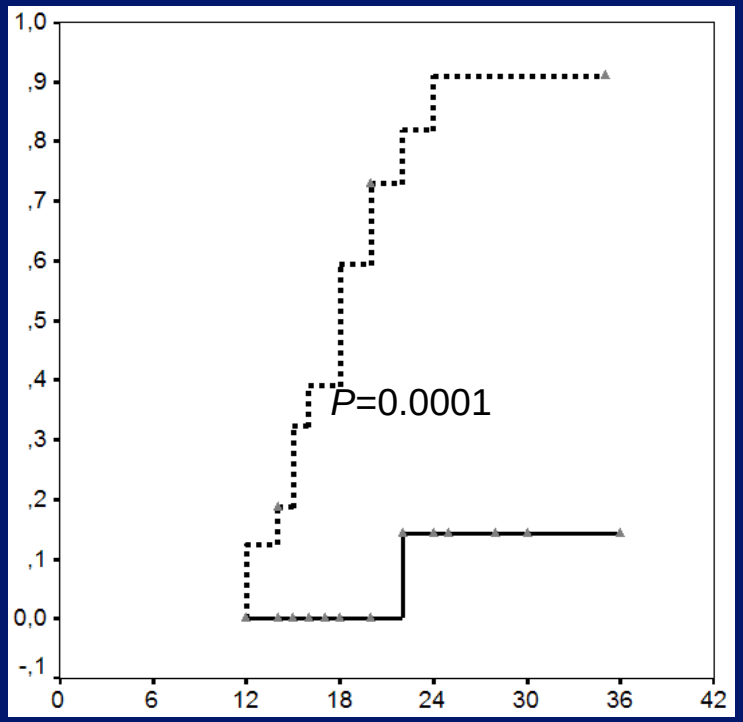
Recommendations	Class[a]	Level[b]
Surgical ablation of AF should be considered in patients with symptomatic AF undergoing cardiac surgery.	IIa	A
Surgical ablation of AF may be performed in patients with asymptomatic AF undergoing cardiac surgery if feasible with minimal risk.	IIb	C
Minimally invasive surgical ablation of AF without concomitant cardiac surgery is feasible and may be performed in patients with symptomatic AF after failure of catheter ablation.	IIb	C

Ablation for AF

Latent Hypertension in AF

292 pts with AF, 32 pts with lone AF
13 out of 14 pts with latent HT: AF recurrence
Katritsis et al. JICE 2005;13:203

Response / partial response
No response



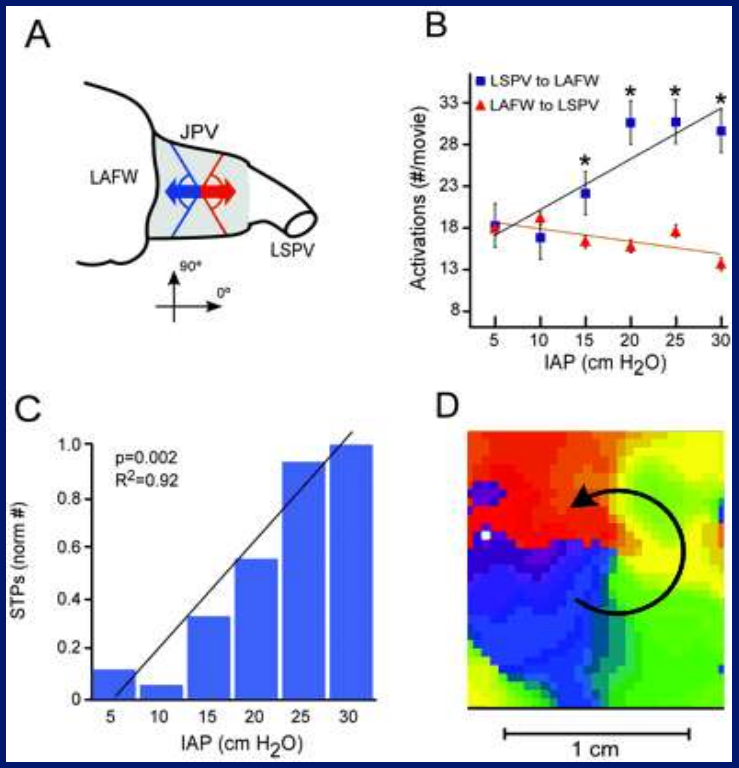
Hypertension

Follow-up in months

Intra-Atrial Pressure Increases Rate and Organization of Waves Emanating From the SPVs During AF

Kalifa et al. Circulation 2003;108:668

Spatio-temporally periodic wavefronts



Intra-atrial pressure

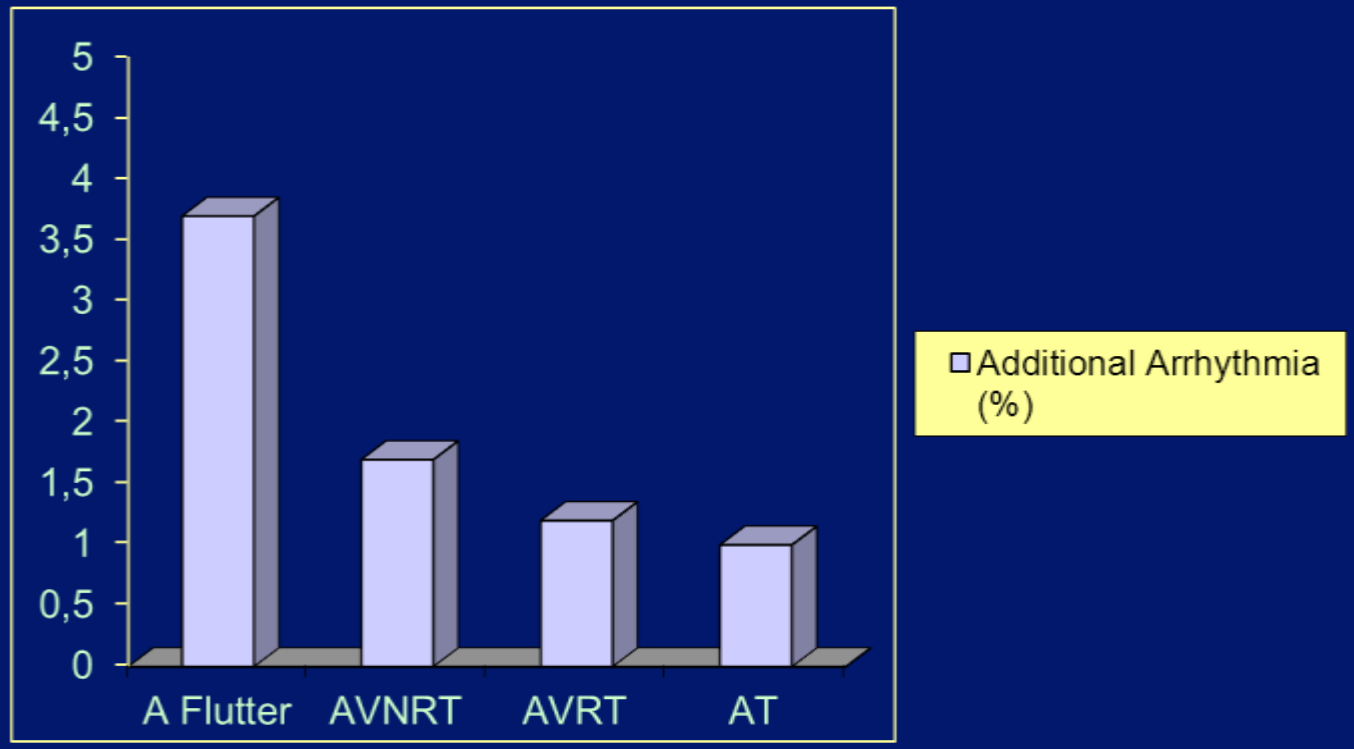
Ablation for AF

Katritsis et al. Europace 2007;9:785-9

EPS is mandatory

409 pts referred for AF ablation

6.7% additional inducible arrhythmia



Up-stream Therapy

ACEIs and ARBs for Primary Prevention

Zografos T, Katritsis D. Pacing Clin Electrophysiol. 2010;33:1270-85

ACEIs and ARBs are beneficial for primary prevention of AF in patients with heart failure,

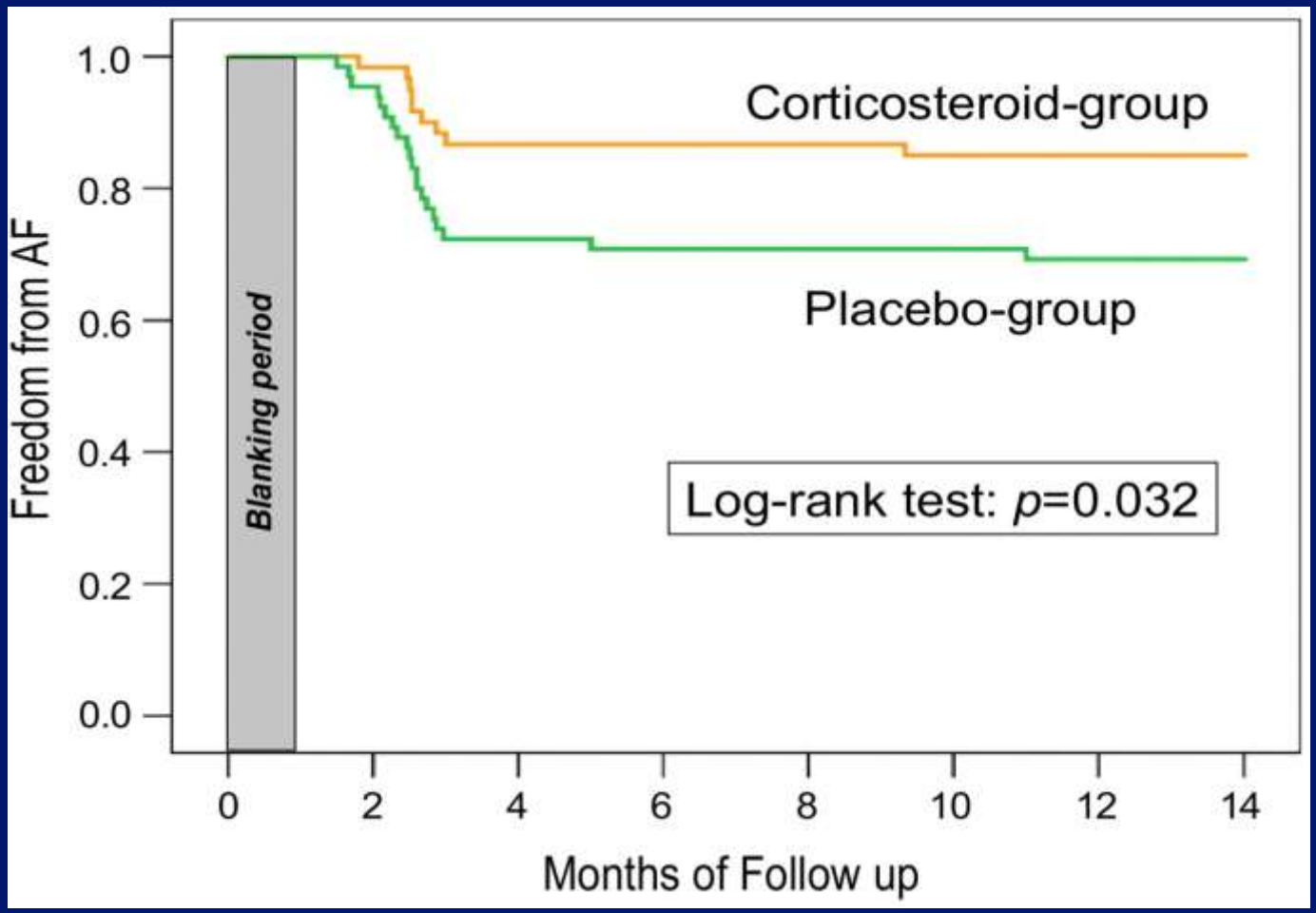
and

for secondary prevention of AF after electrical cardioversion.

Up-stream Therapy

125 pts after cardioversion

Koyama, T. et al. J Am Coll Cardiol 2010;56:1463-1472

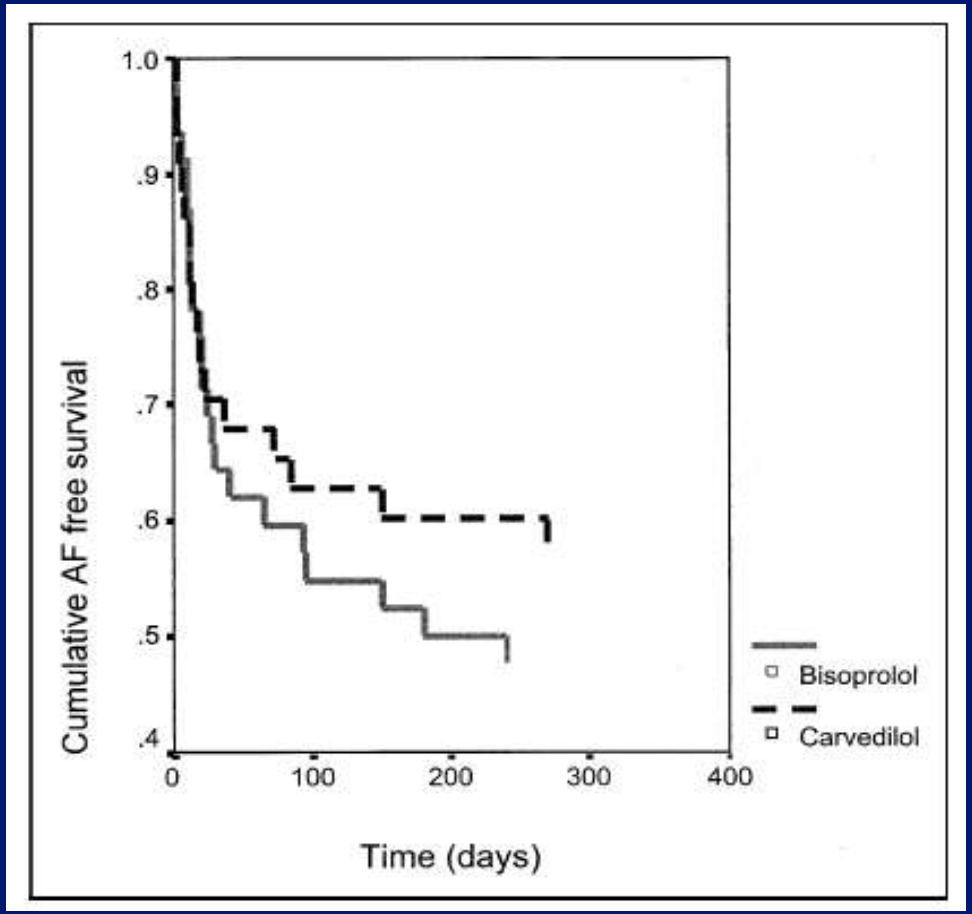


Ablation for AF

Beta blockers in AF

Katritsis et al. Am J Cardiol 2003;92:1116

Comparison of bisoprolol vs carvedilol for SR maintenance after cardioversion of persistent AF



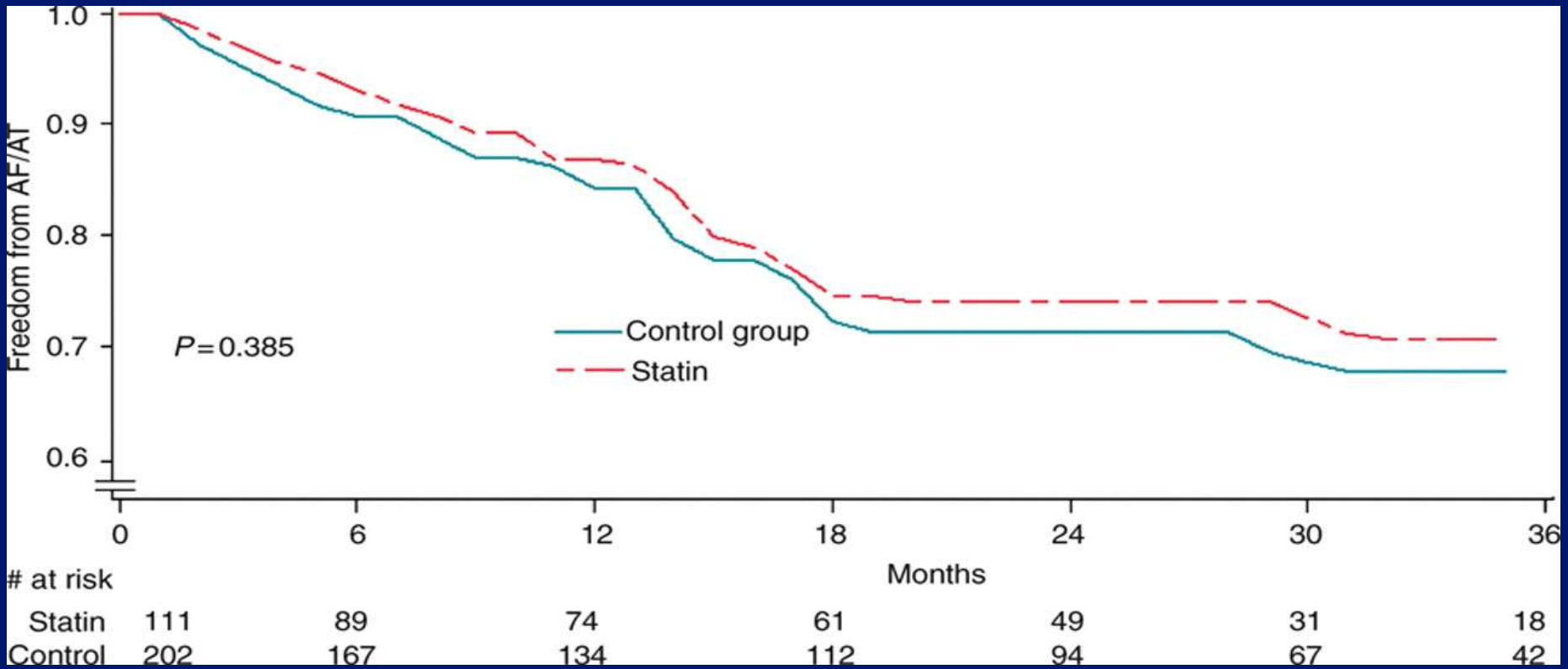
Up-stream Therapy

No pleiotropic effects

Freedom from AF/AT, according to statin use and control population.

518 female postmenopausal pts

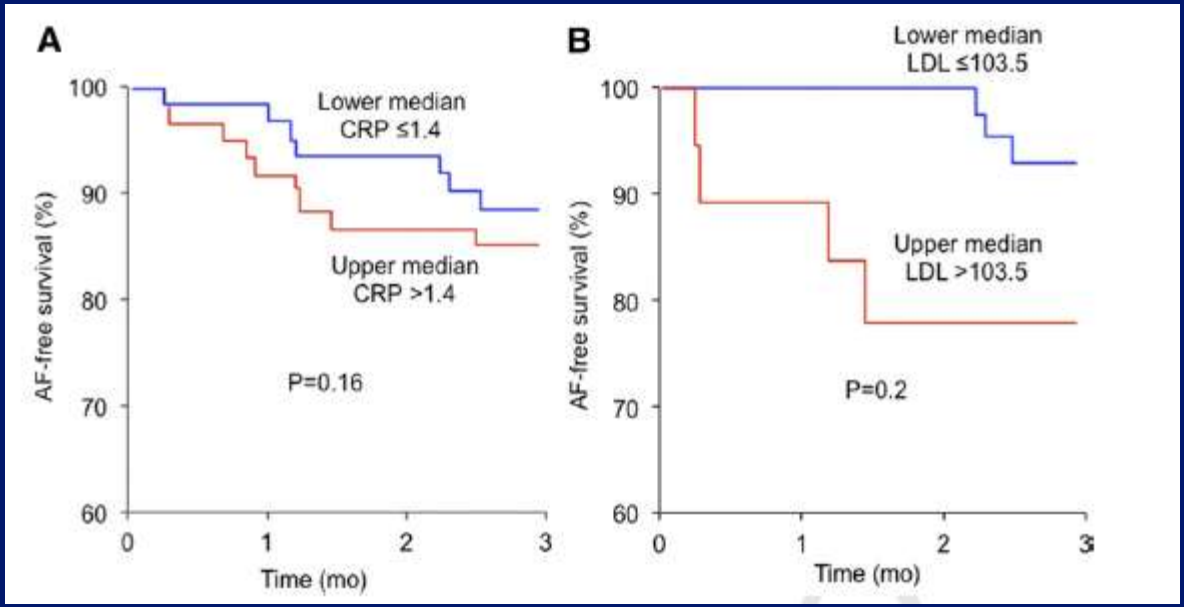
Patel D et al. Europace 2010;12:322-330



Up-stream Therapy

Atorvastatin following PVI

Suleiman et al. HeartRhythm (E-Pub)



ΥΠΟΤΡΟΠΗ ΚΟΛΠΙΚΗΣ ΜΑΡΜΑΡΥΓΗΣ ΚΑΤΟΠΙΝ ABLATION

Συμπεράσματα

1. Αναζήτηση άλλων αιτίων και θεώρηση επικουρικής θεραπείας
2. Τα φάρμακα ως μόνη θεραπεία δεν επαρκούν
3. Η χειρουργική αντιμετώπιση ίσως ενδείκνυται μόνο σε περίπτωση χειρουργείου γιά άλλη αιτία
4. Επανάληψη ablation ενδείκνυται μετά προσεκτική επιλογή ασθενών και μεθόδου