Long-Term Atrial Fibrillation Progression: What We Know in 2014

Advances in Cardiac Arrhythmias and Great Innovations in Cardiology
XXVI Giornate Cardiologiche Torinesi
Turin, 23-25 October 2014

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Department of Medical Sciences
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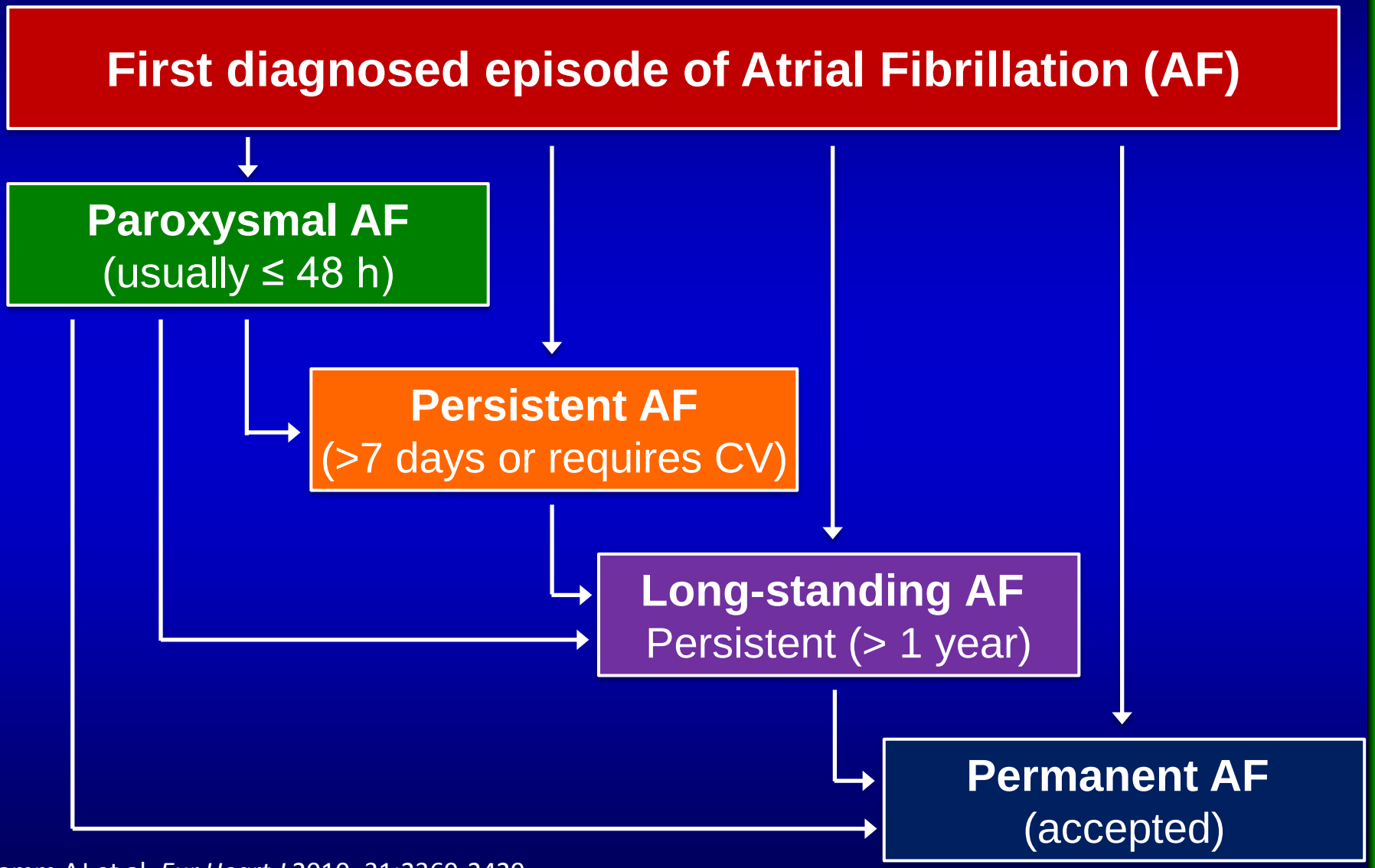
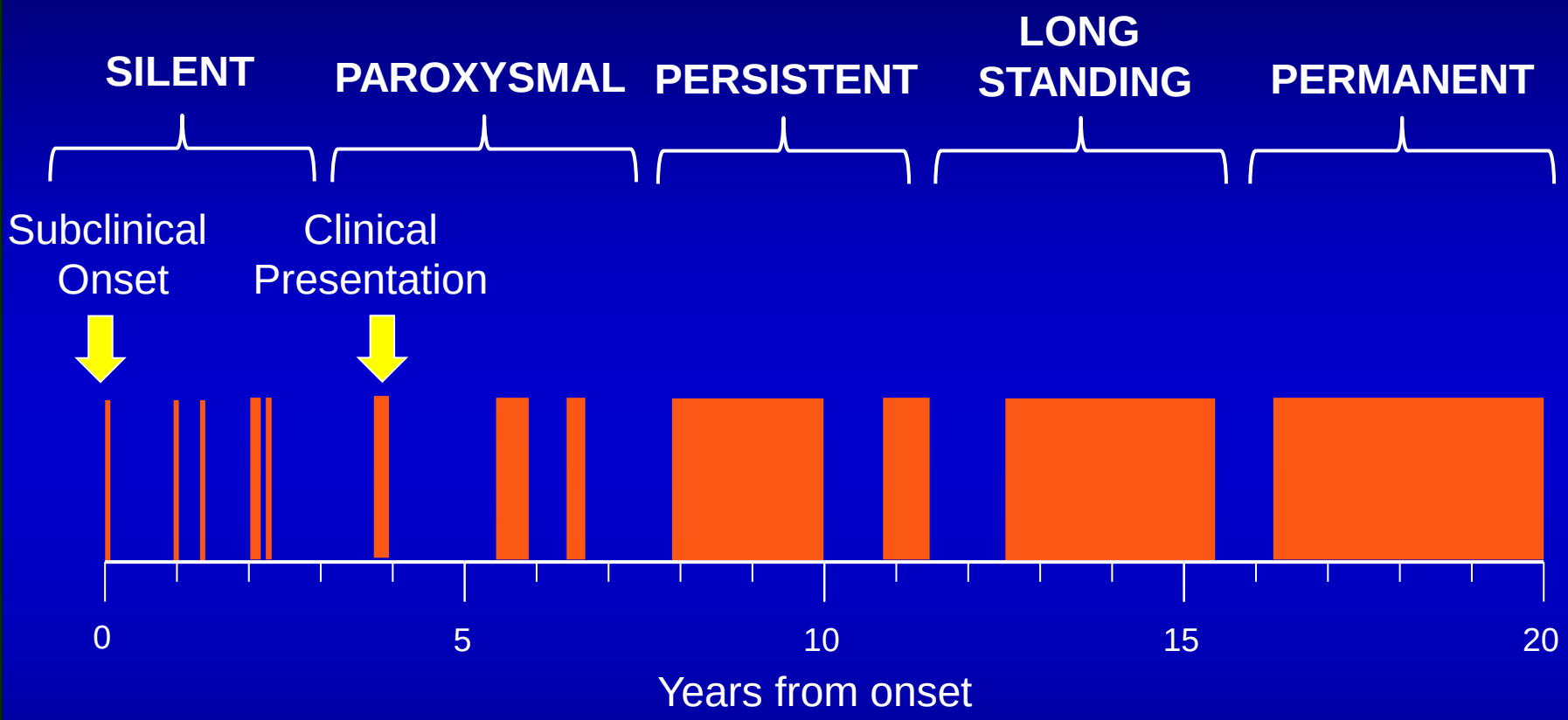
I HAVE NO CONFLICT OF INTEREST TO DISCLOSE

Atrial Fibrillation Classification



Camm AJ et al. *Eur Heart J* 2010; 31:2369-2429

Natural Time Course of AF



What is the rate of progression and is it clinically relevant?

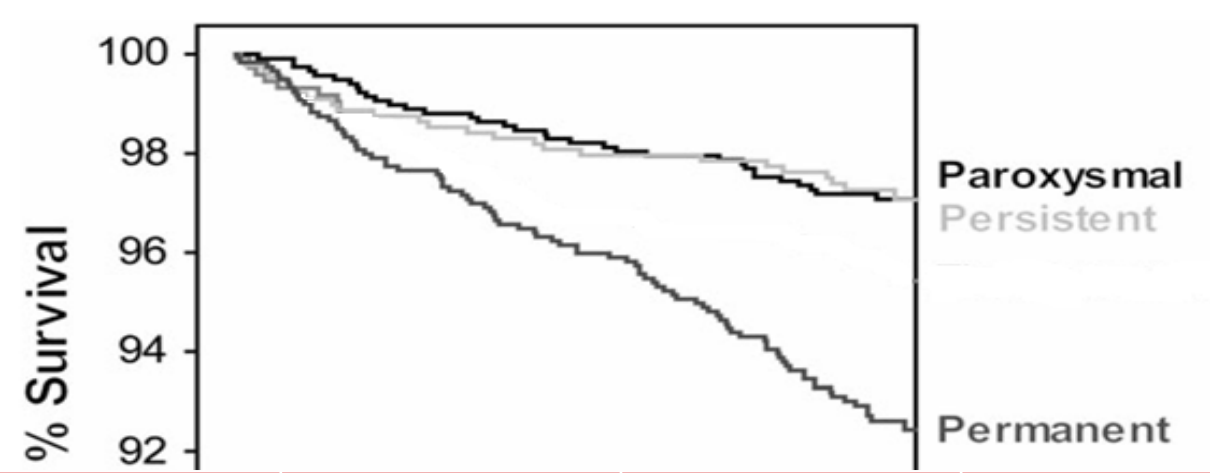
Progression Toward Permanent AF

Study	Pts	AF Subtype	AF Duration at inclusion	FUP	AF Progression Per-Year (%)
Belgrade AF Study 2012	346	1st AF detection; Parox 70%; Pers 22%	New onset	12	2.8%
Danish Study 1986	426	Paroxysmal	New onset	9	3.7%
CARAF 2005	757	Paroxysmal	New onset	8	5%
Abe 1997 (Osaka)	122	Paroxysmal; lone AF 21%	<6 months	2.2	5.5%
Al-Khatib 2000 (Dhuram)	231	Paroxysmal; lone AF 42%	≥ 1 document. episode	4	8%
European Heart Survey 2010	1219	Paroxysmal; Lone AF 17%	New onset	1	8%
RECORD-AF 2012	2137	Paroxysmal; Lone AF 20%	≤1 Year	1	9%

Average AF Progression Rate ≈ 5% per-year

Clinical Impact of AF Progression

AF Euro Heart Survey – 4192 pts, 1 year FU

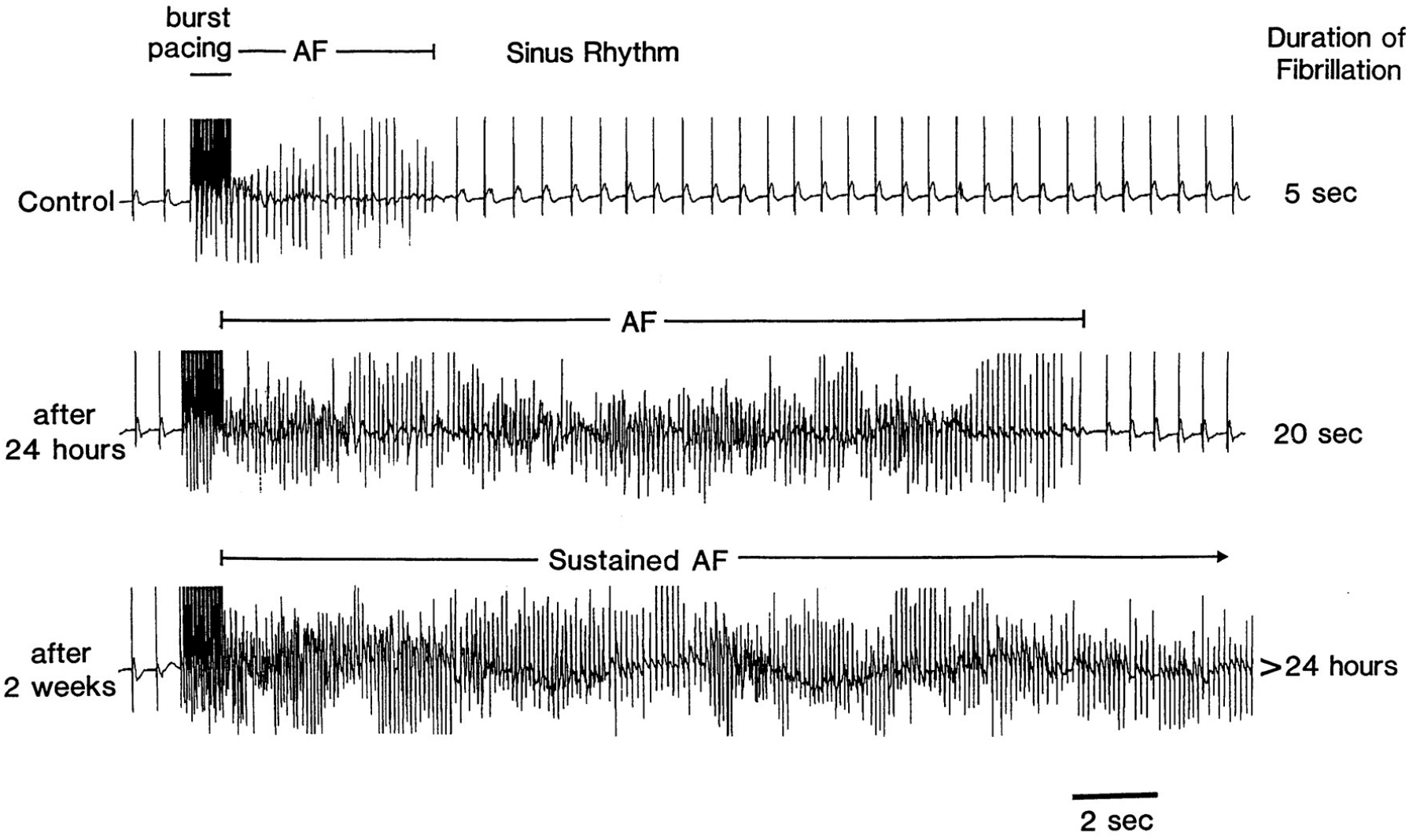


	Paroxysmal N=1170	Persistent N=886	Permanent N=1126	P-Value
All-cause death	43 (3.5)	27 (3.0)	100 (8.2)	<0.001
CV-death	15 (1.3)	19 (2.1)	43 (3.6)	0.001
Heart Failure Events	109 (9.6)	75 (8.5)	195 (16.6)	<0.001
Ischaemic stroke	22 (1.9)	11 (1.2)	19 (1.6)	0.582

Adapted from Nieuwlaat R et al. *Eur Heart J* 2008; 29:1181-1189

What Causes AF Progression?

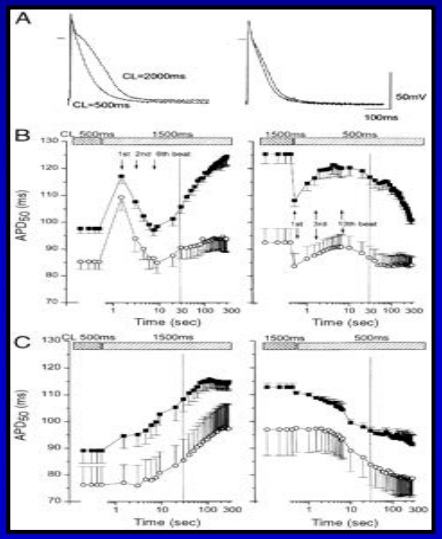
AF is a Self-Perpetuating Condition



Wijffels MC et al. *Circulation* 1995;92:1954-1968

AF-Related Remodelling

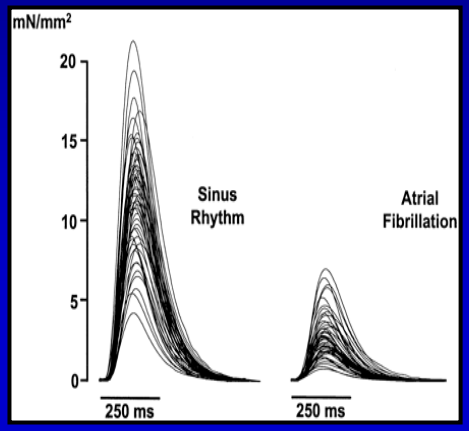
Electrical



AERP shortening and lack of adaptation, ↓ atrial conduction velocity, Intracellular Ca^{2+} oscillations

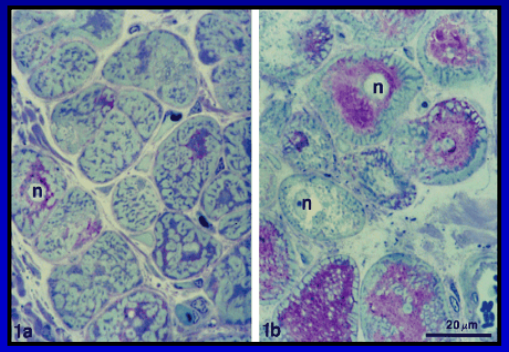
REVERSIBLE

Contractile



REVERSIBLE BUT TIME DEPENDENT

Structural

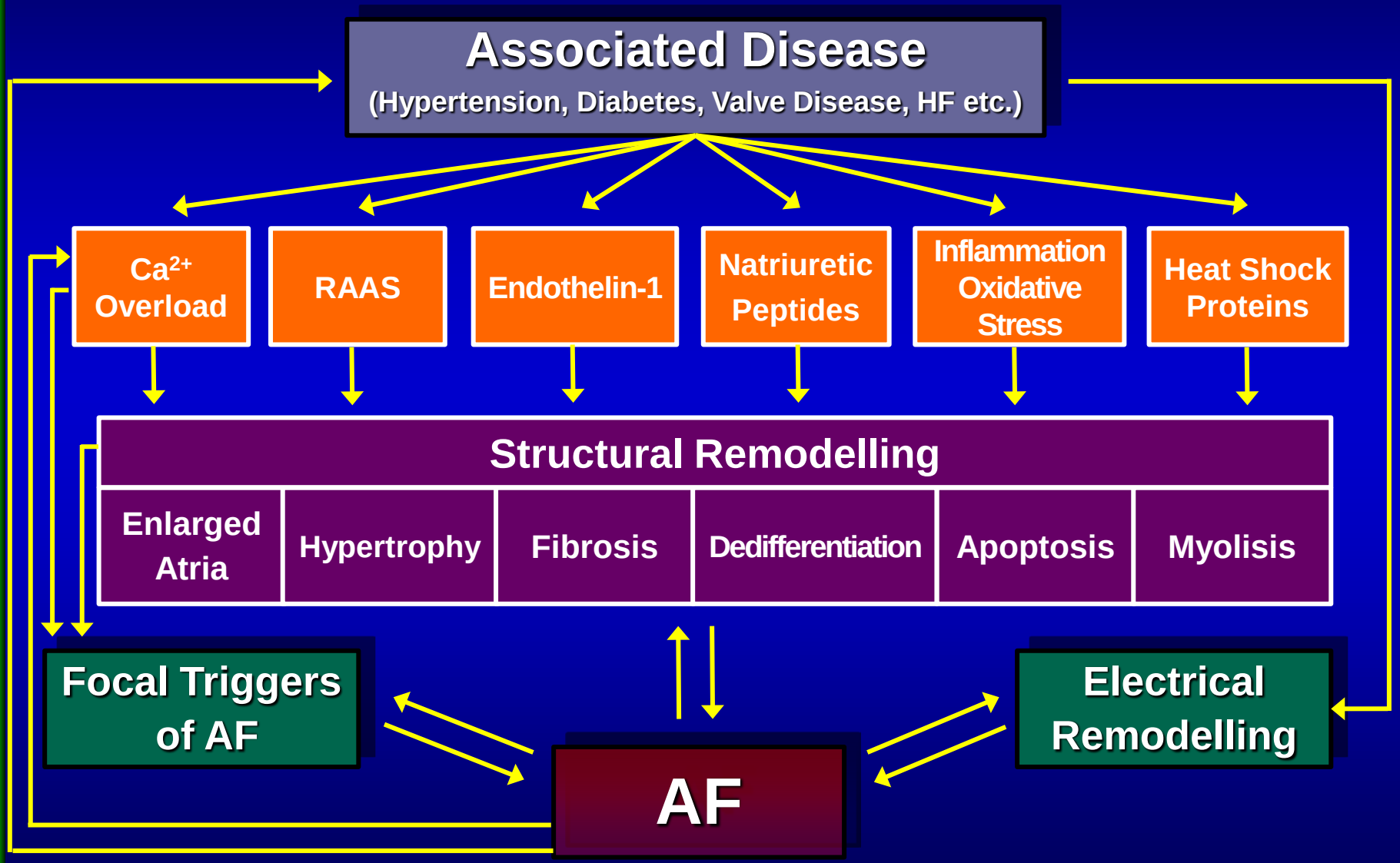


Apoptosis, Fibroblast proliferation, Collagen Content ↑, Fibrosis, Structural Disarray

NOT COMPLETELY REVERSIBLE

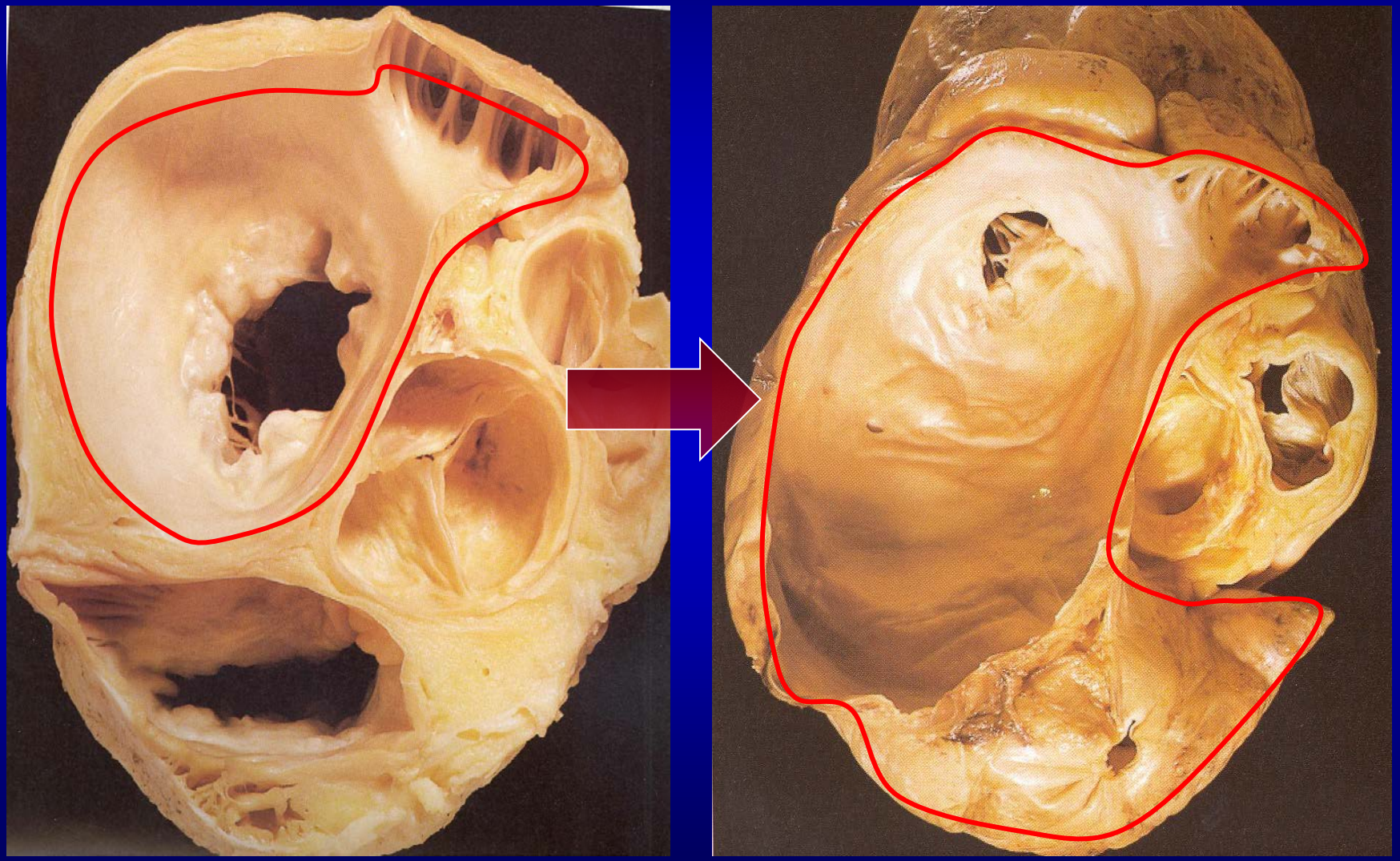
Adapted from Allessie M et al. *Cardiovasc Res* 2002; 54: 230-246

Underlying Disease and Remodelling



Adapted from De Jong AM et al. *Cardiovasc Res* 2011; 89: 754-765

Left Atrium Remodelling



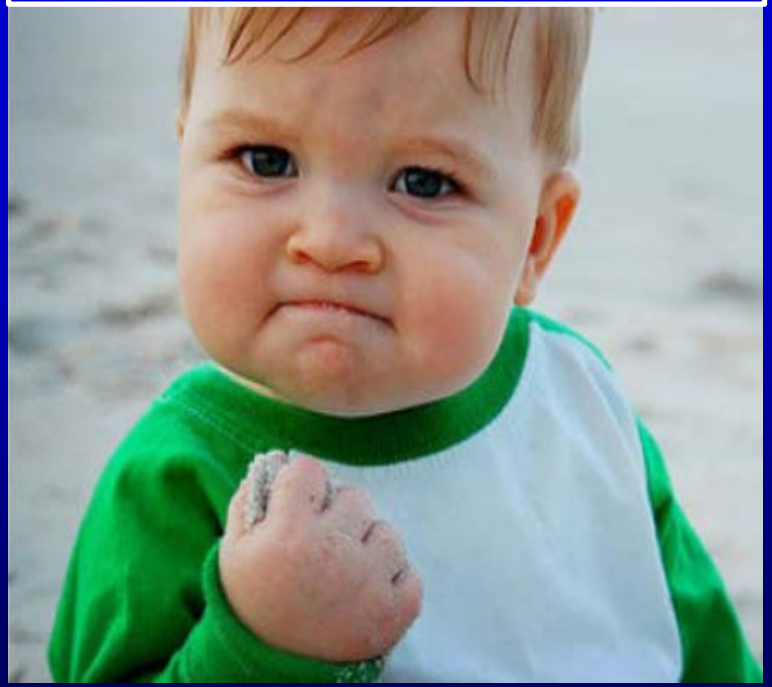
Which Factors Influence AF Progression Rate?

Physician's and Patient's Belief

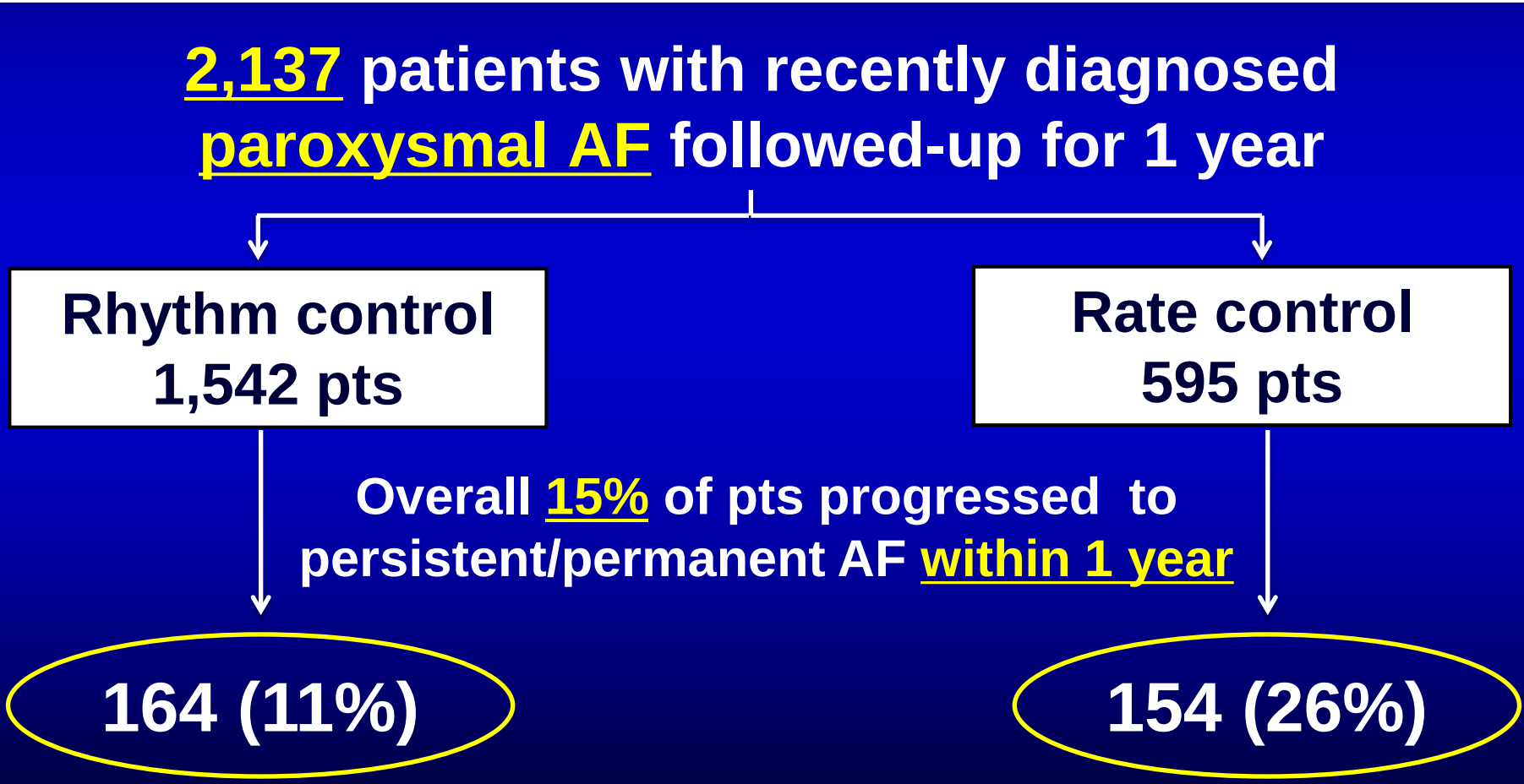
Restoring Sinus Rhythm to Prevent AF Progression…

…WHY BOTHER?

…WE CAN DO IT !



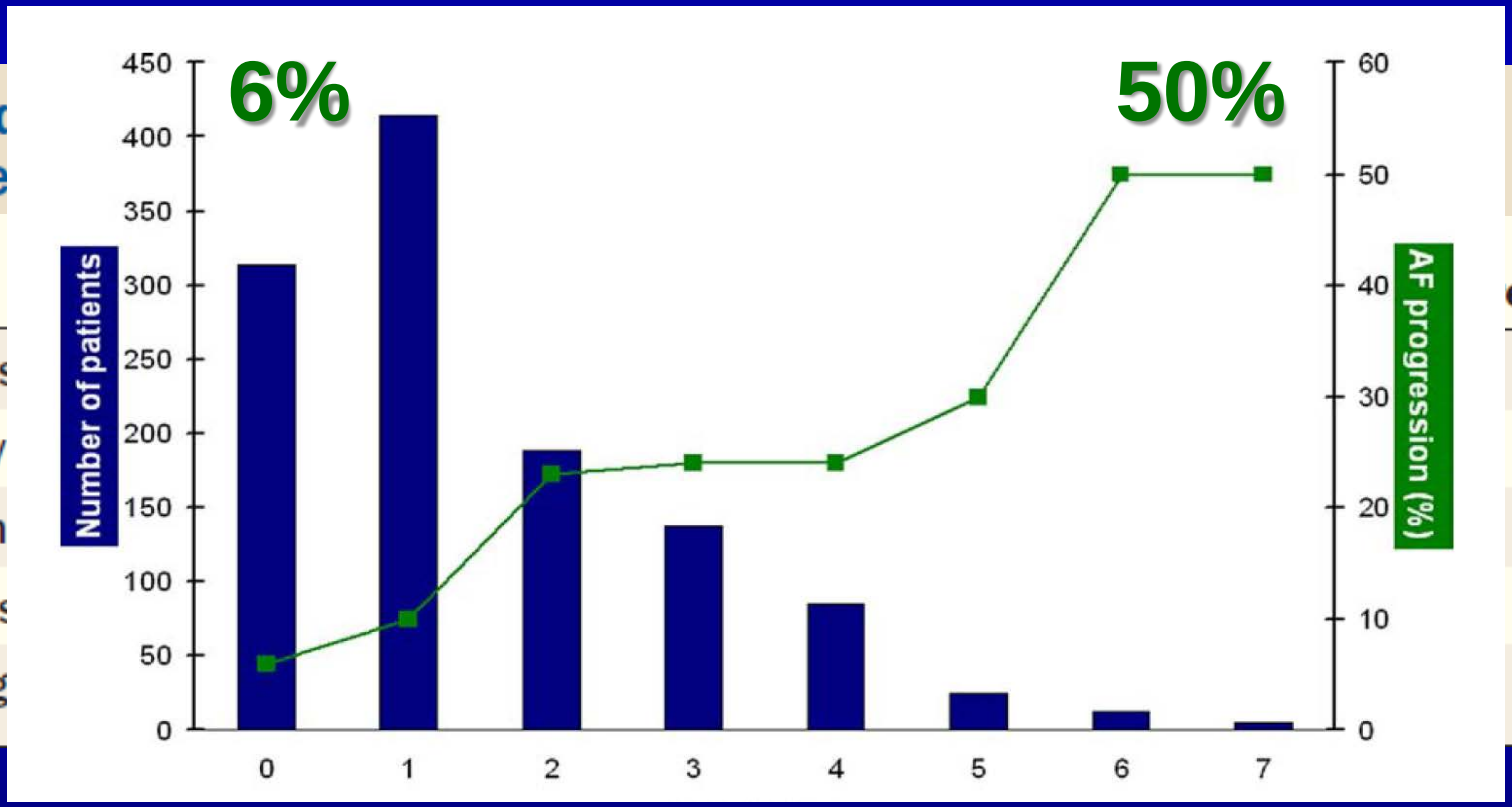
Progression of atrial fibrillation in the REgistry on Cardiac rhythm disORDers assessing the control of Atrial Fibrillation cohort: Clinical correlates and the effect of rhythm-control therapy



De Vos CB et al. *Am Heart J* 2012;163:887-93

Clinical Correlates of AF Progression

1 Year AF progression in 1219 paroxysmal AF pts



HATCH Score (Min 0 – Max 7)

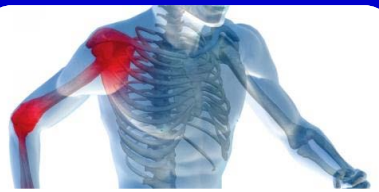
De Vos CB et al. *J Am Coll Cardiol* 2010;55:725-31

Other Risk Factors Associated With AF Progression

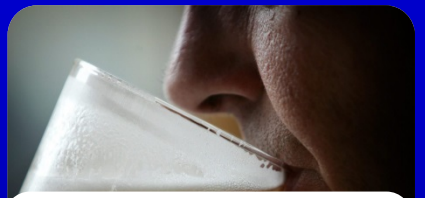
DIABETES
50% ↑ AF Risk

OBESITY
5% ↑ AF Risk per
1-unit BMI ↑

AF



INFLAMMATION
36% ↑ AF Risk
per CRP tertile



ALCOHOL
8% ↑ AF Risk per
10-g daily

SLEEP APNEA
In up to 50%
of AF pts

Original Investigation

Effect of Weight Reduction and Cardiometabolic Risk Factor Management on Symptom Burden and Severity in Patients With Atrial Fibrillation

150 pts with symptomatic AF (paroxysmal/persistent) BMI > 27

Weight Management N = 75
8 weeks very low-calorie diet
Low-glycaemic index meals
Low-intensity exercise plan
Goal-directed clinic visits

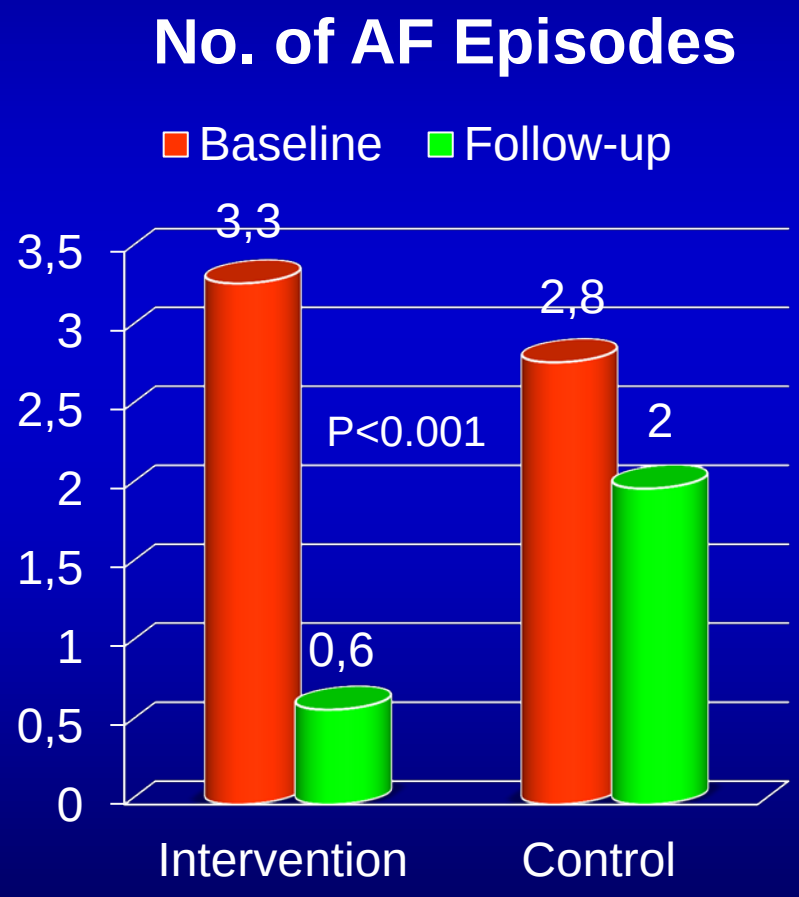
General Lifestyle Advice N = 75
Nutrition and exercise advice

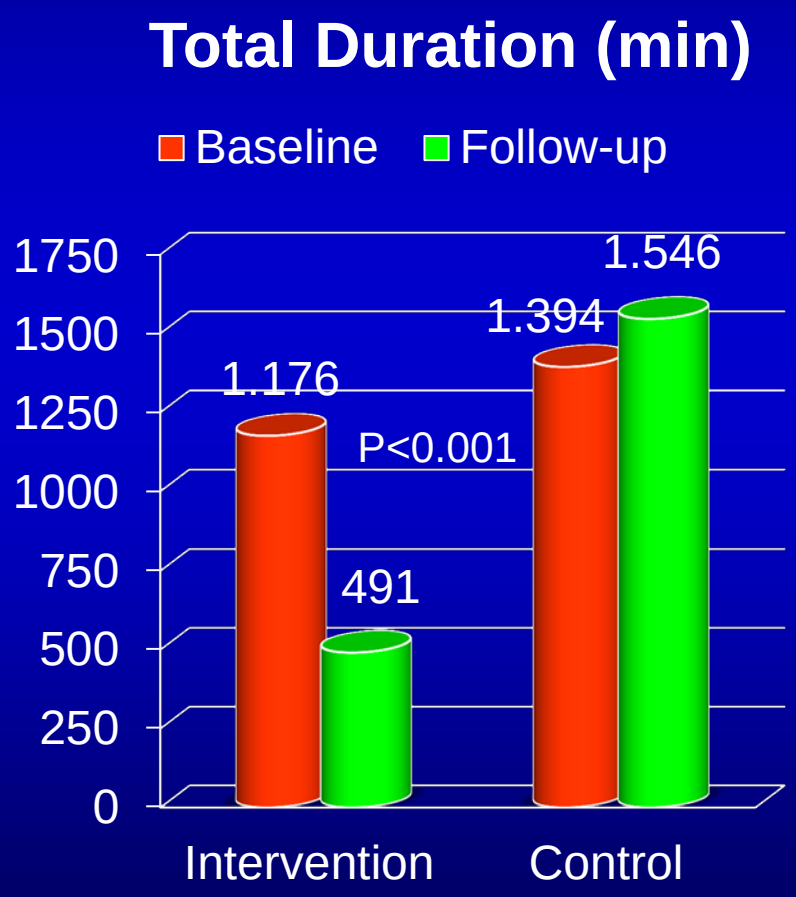
Outcome: Atrial Fibrillation Symptoms Burden, Severity and Recurrence

Abed HS. et al. *JAMA* 2013;310: 2050-2060

Original Investigation

Effect of Weight Reduction and Cardiometabolic Risk Factor Management on Symptom Burden and Severity in Patients With Atrial Fibrillation





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Original Investigation

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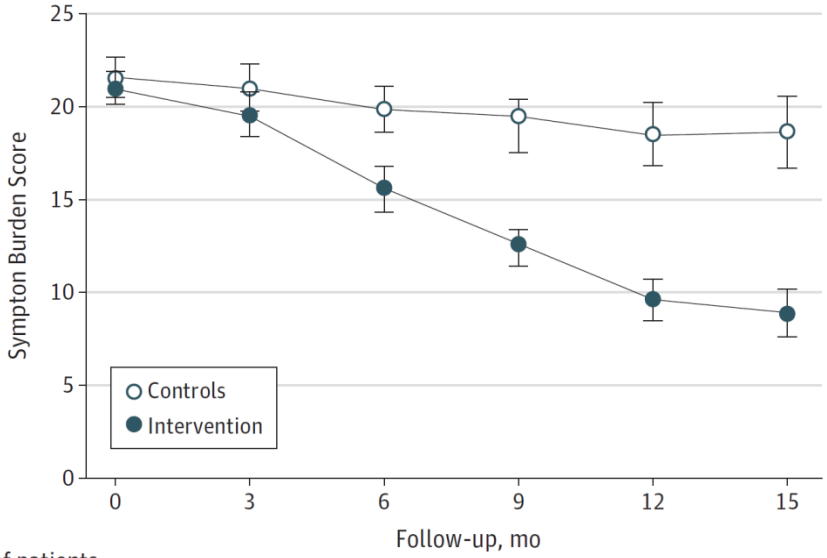
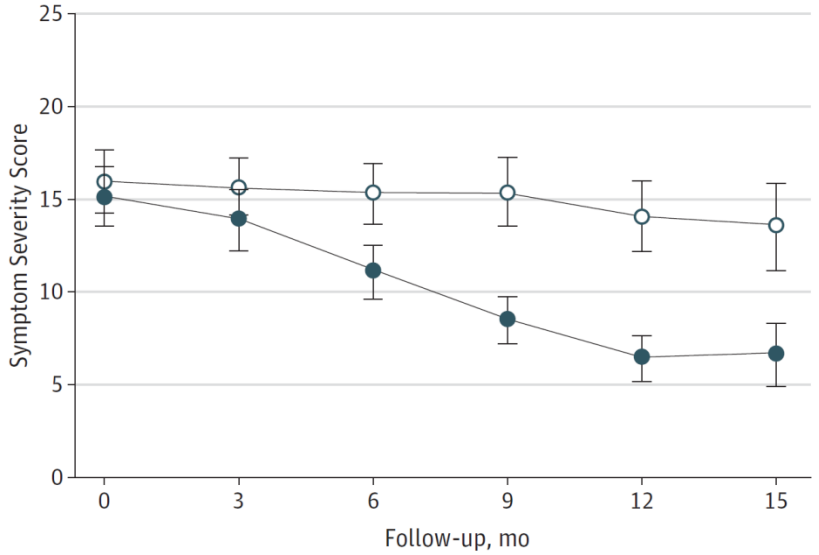
Symptom Burden Score (AFSS)



No. of patients

Controls	75	75	72	61	52	39
Intervention	75	75	75	73	57	42

Symptom Severity Score (AFSS)



	75	75	72	61	52	39
	75	75	75	73	57	42

Abed HS. et al. *JAMA* 2013;310: 2050-2060

Which Therapeutic Strategies Can Be Used To Halt or Delay AF Progression?

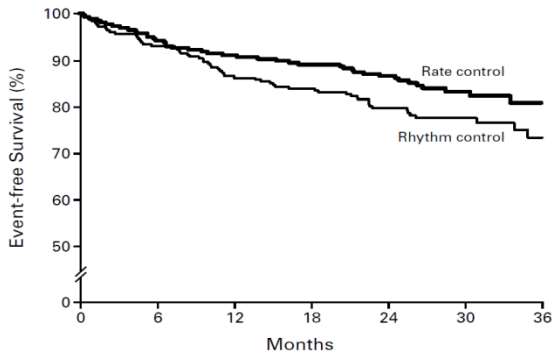
Antiarrhythmic Drugs and Electrical Cardioversion

Rhythm vs. Rate Control Trials

Trial	Inclusion criteria	Primary outcome Parameter	Patients reaching primary outcome (n)		
			Rate ctrl	Rhytm ctrl	P
PIAF (2000) 252 Patients	Persistent AF (7-360 days)	Symptomatic improvement	76/125 (60.8%)	70/127 (55.1%)	0.32
AFFIRM (2002) 4060 Patients	Paroxysmal AF or persistent AF, age ≥65 years, or risk of stroke or death	All-cause mortality	310/2027 (25.9%)	356/2033 (26.7%)	0.08
RACE (2002) 522 Patients	Persistent AF or flutter for <1 year and 1-2 cardioversions over 2 years and oral anticoagulation	Composite: cardiovascular death, CHF, severe bleeding, pacemaker implantatation, thrombo-embolic events, severe adverse effects of antiarrhythmic drugs	44/256 (17.2%)	60/266 (22.6%)	0.11
STAF (2003) 200 Patients	Persistent AF (>4 weeks and <2 years), LA size >45 mm, CHF NYHA II-IV, LVEF <45%	Composite: overall mortality, cerebrovascular complications, CPR, embolic events	10/100 (10.0%)	9/100 (9.0%)	0.99
HOT CAFÈ (2004) 205 Patients	First clinically overt persistent AF (≥7 days and <2 years), age 50-75 years	Composite: death, thrombo-embolic events; intracranial/major haemorrhage	1/101 (1.0%)	4/104 (3.9%)	>0.71
AF-CHF (2008) 1376 Patients	LVEF ≤35%, symptoms of CHF, history of AF (≥6 h or DCC <last 6 months)	Cardiovascular death	[illegible] (25%)	[illegible] (27%)	0.59

Low Maintenance Rate of Sinus Rhythm

RACE Trial (N=522)



After a mean FUP of 2.3 years:

- **39% SR in the rhythm control arm**
- **10% SR in the rate control arm**

Patients in the Late State of the Disease

- **PIAF, RACE, STAF enrolled pts with persistent AF**
- **In RACE all pts had previously undergone cardioversion**
- **In AF-CHF trial all had structural heart disease,**
  2/3 of pts had persistent AF, 46% had AF>6 months

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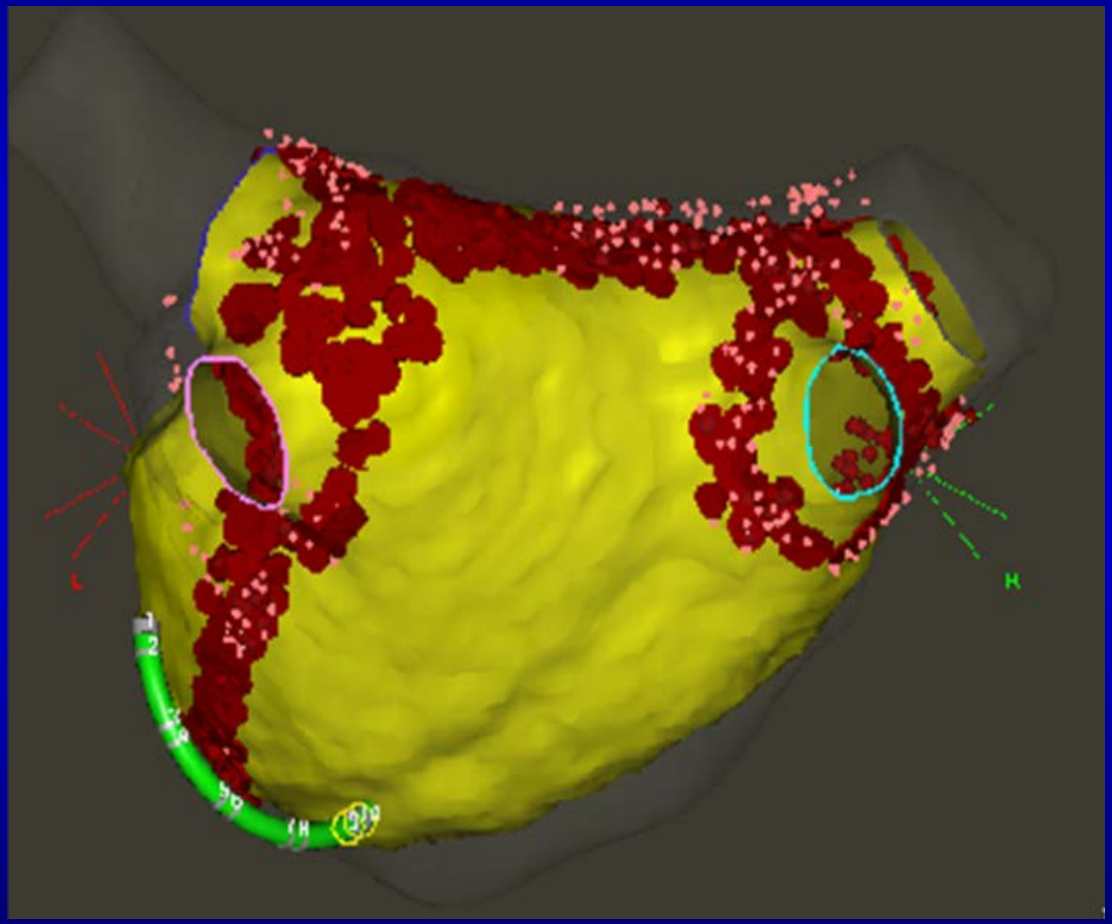
AF-CHF (2008) 1376 Patients	LVEF ≤35%, symptoms of CHF, history of AF (≥6 h or DCC <last 6 months)	Cardiovascular death	175/1376 (25%)	199/1376 (27%)	0.59
J-RHYTHM (2009) 823 Patients	Paroxysmal AF	Composite of total mortality, symptomatic cerebral infarction, systemic embolism, major bleeding, hospitalization for heart failure, or	89/405 (22.0%)	64/418 (15.3%)	0.012

Wise Old Saying…

AF Transcatheter Ablation



Impact of Transcatheter Ablation on AF Progression

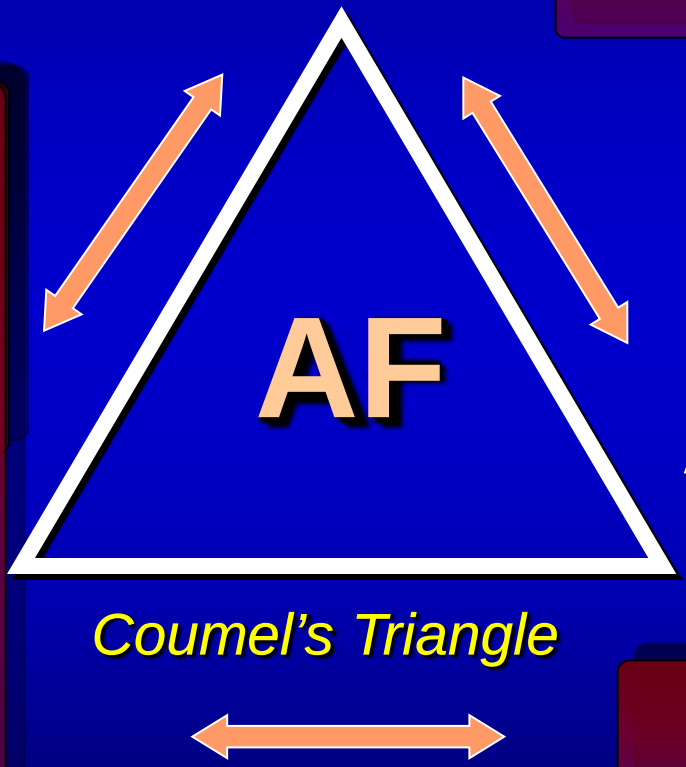
Substrate

Structural:
Left atrium dilation.
Atrial fibrosis.
Atrial inflammation.
Myocytes hypertrophy.
Loss of connexins

Electrical:
Shortening and dispersion of refractory periods (ERP).
Lack of ERP adaptation to heart rate increase.
Intra-atrial conduction delay.
Functional conduction block

Trigger

PV Foci
Rotors



Coumel's Triangle

Autonomic Nervous System

Vagal tone
Adrenergic drive

Courtesy of Prof. Gaita

Long-term Outcomes of Catheter Ablation of Atrial Fibrillation: A Systematic Review and Meta-analysis

Anand N. Ganesan, MBBS, PhD; Nicholas J. Shipp, PhD; Anthony G. Brooks, PhD; Pawel Kuklik, PhD; Dennis H. Lau, MBBS, PhD; Han S. Lim, MBBS, PhD; Thomas Sullivan, BMa, CompSc; Kurt C. Roberts-Thomson, MBBS, PhD; Prashanthan Sanders, MBBS, PhD

19 Studies – 6167 pts undergoing AF ablation

SR after multiple proc
- 1 year 86%
- 5 years 78%

SR after single proc
- 1 year 67%
- 5 years 53%

J Am Heart Assoc 2013; 2:e004549

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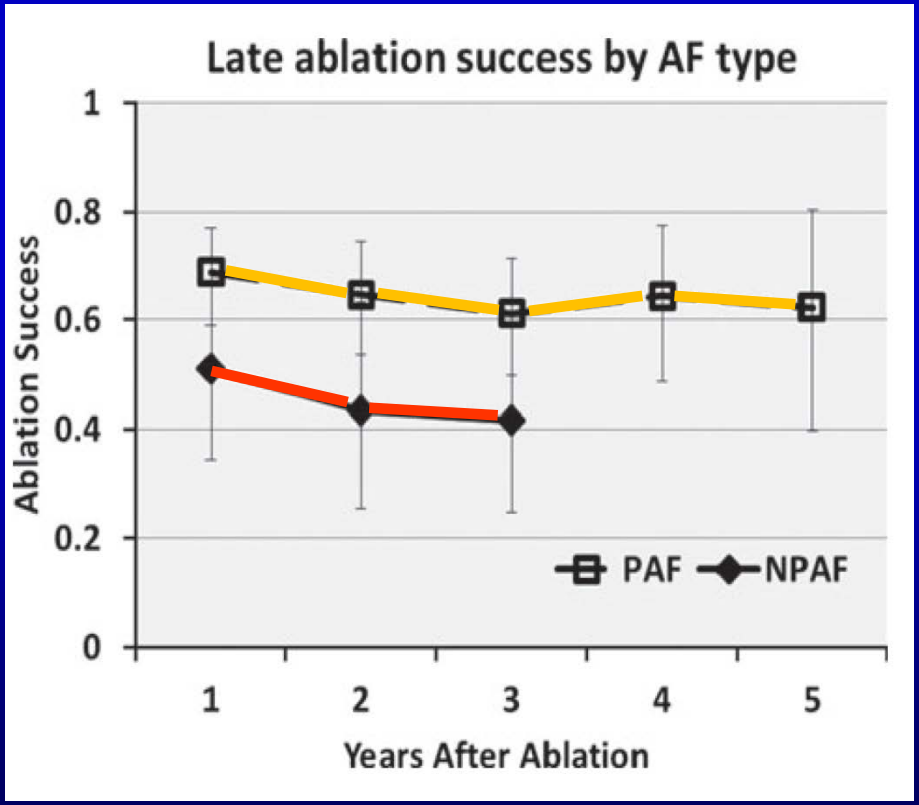


Paroxysmal AF
- 1 year 69%
- 5 years 62%

NON-Paroxysmal AF
- 1 year 51%
- 5 years 42%

J Am Heart Assoc 2013; 2:e004549

Long-term progression from paroxysmal to permanent atrial fibrillation following transcatheter ablation in a large single-center experience

(Heart Rhythm 2014;11:777–782)

Marco Scaglione, MD,* Cri… ,† Davide Sardi, MD,*
Luca Gaido, MD,† Matteo … ,† Carla Giustetto, MD,†
Davide Castagno, MD,† Fe… D,* Fiorenzo Gaita, MD†

889 Patients
Referred for AF TC ablation
2001-2010

Mean Age Years	57
Hypertension %	46
Structural CMP %	22
Lone AF %	30

Paroxysmal AF
474 (53.3%) pts

Persistent AF
360 (40.5%) pts

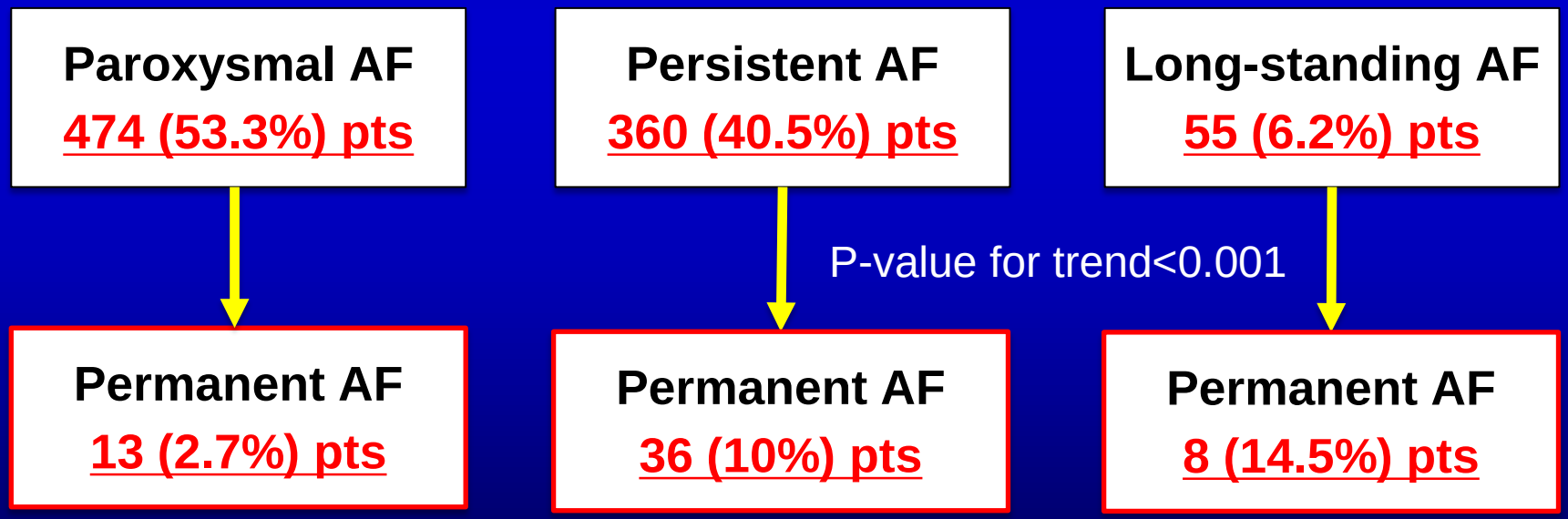
Long-standing AF
55 (6.2%) pts

Median Follow-up = 64 months (IQR 41-84)

Long-term progression from paroxysmal to permanent atrial fibrillation following transcatheter ablation in a large single-center experience

Progression to permanent AF = 57 (6.4%) pts

Overall 276 (31%) pts underwent redo procedures



Scaglione et al. *Heart Rhythm* 2014;11: 777-782

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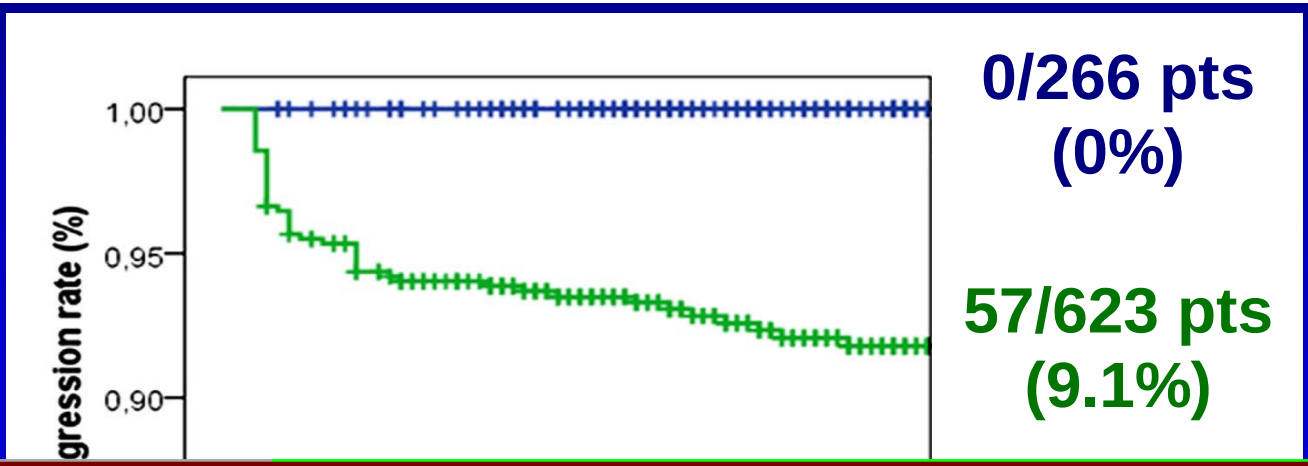


0/266 pts (0%)

57/623 pts (9.1%)

Clinical Features	No AF Progression (n= 832)	AF Progression (n = 57)	Multivariable Analysis OR (95% CI)
Structural CMP	**167 (20%)**	**30 (53%)**	**11.3 (2.6–48.0) p<0.001**
Long-standing AF	**47 (85%)**	**8 (15%)**	**1.6 (1.2–2.1) p<0.001**

Adjusted for: age, hyperthyroidism, CHA_2DS_2VASc score, baseline comorbidities, left atrial enlargement

Scaglione et al. *Heart Rhythm* 2014;11: 777-782

Conclusions

The natural history of AF is characterized by progression toward permanent form which is associated with worse outcome

Progression is not systematic being influenced by age, comorbidities, physician's and patient's belief

The potential prognostic impact of an early rhythm control strategy must be investigated in randomized clinical trials


Thank you for your attention!

Back-up Slides

Cardiac Pacing and AF Progression

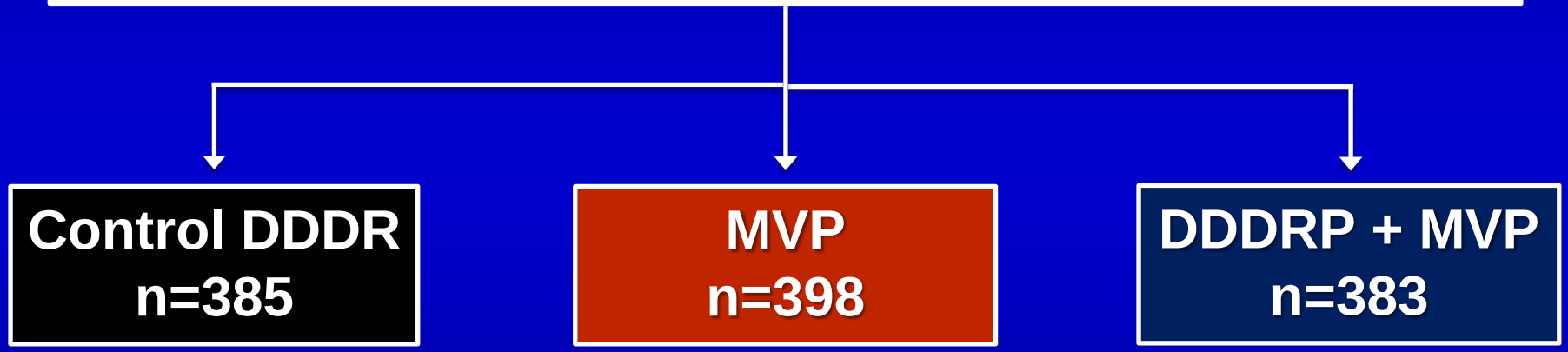
Which is the optimal pacing mode in sinus node dysfunction and paroxysmal/persistent AF?

Atrial antitachycardia pacing and managed ventricular pacing in bradycardia patients with paroxysmal or persistent atrial tachyarrhythmias: the MINERVA randomized multicentre international trial

Boriani G. et al. *Eur Heart J* 2014;35: 2352-2362

The MINERVA randomized multicentre international trial

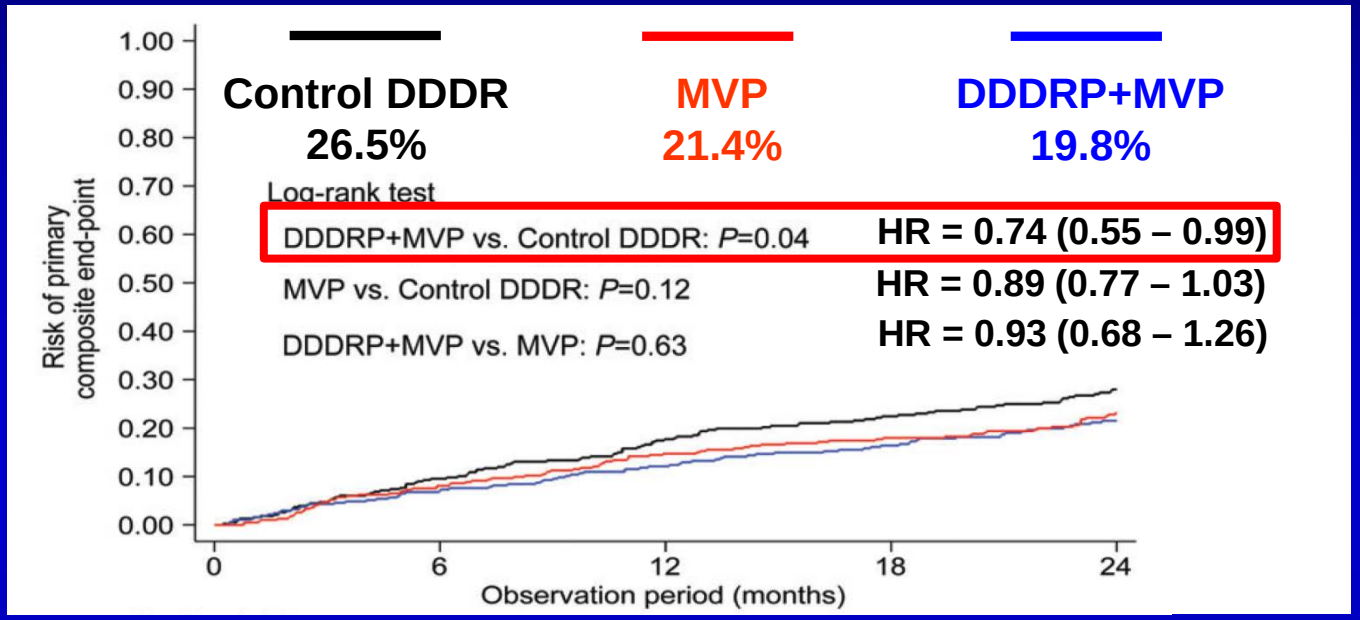
1166 pts with bradycardia and paroxysmal/persistent atrial tachyarrhythmias undergoing PM implantation



Primary outcome: 2-years incidence of a combined endpoint of Death OR CV-Hospitalization OR Progression to permanent AF

Boriani G. et al. *Eur Heart J* 2014;35: 2352-2362

The MINERVA randomized multicentre international trial



Endpoint	Control DDDR n=385	MVP n=398	DDDRP+MVP n=383
Death or CV-Hosp or Permanent AF	102 (26.5)	85 (21.4)	76 (19.8)
Death	20 (5.2)	19 (4.8)	16 (4.2)
CV-Hospitalization	60 (15.6)	49 (12.3)	53 (13.8)
Permanent AF	33 (8.6)	27 (6.8)	13 (3.4)

Boriani G. et al. *Eur Heart J* 2014;35: 2352-2362

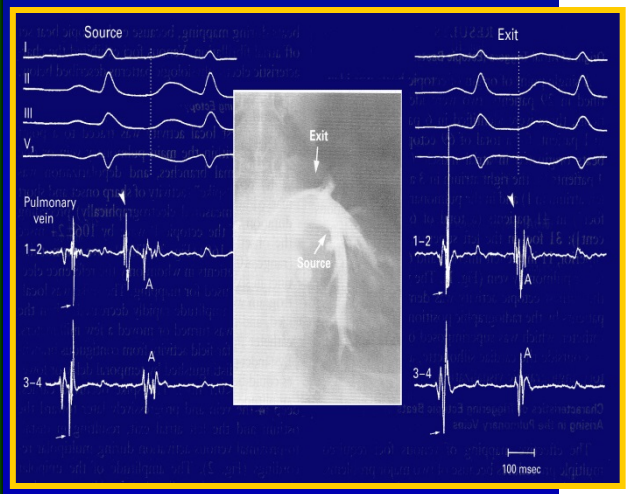
AF duration relates to recurrences following ablation

Baseline variable	*P*	Hazard ratio	95% Confidence interval
Predictors of arrhythmia recurrence after the index procedure:			
Female gender	.001	0.092	0.022–0.386
Duration of persistent AF >6 months	.001	1.644	1.210–2.235
No. of long-lasting persistent AF	.049	1.548	1.003–2.389
Congestive heart failure	.001	10.903	2.602–45.694

AF duration > 6 months
risk of recurrences + 64%

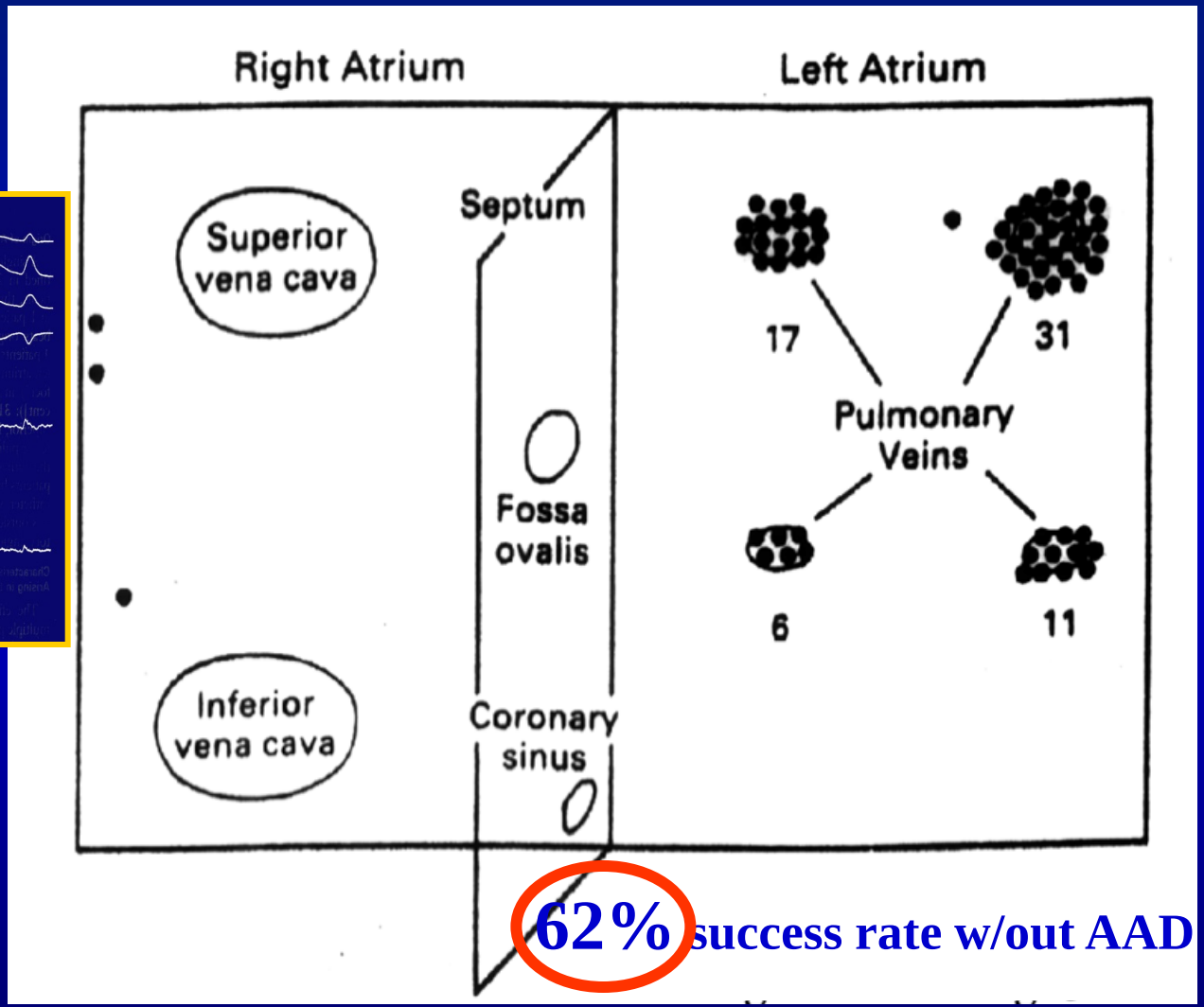
Rostock Heart Rhythm 2011. Balk JCE 2010.
O'Neill Eur Heart J 2009. Della Bella Europace 2005

Cornerstone of AF ablation: trigger elimination



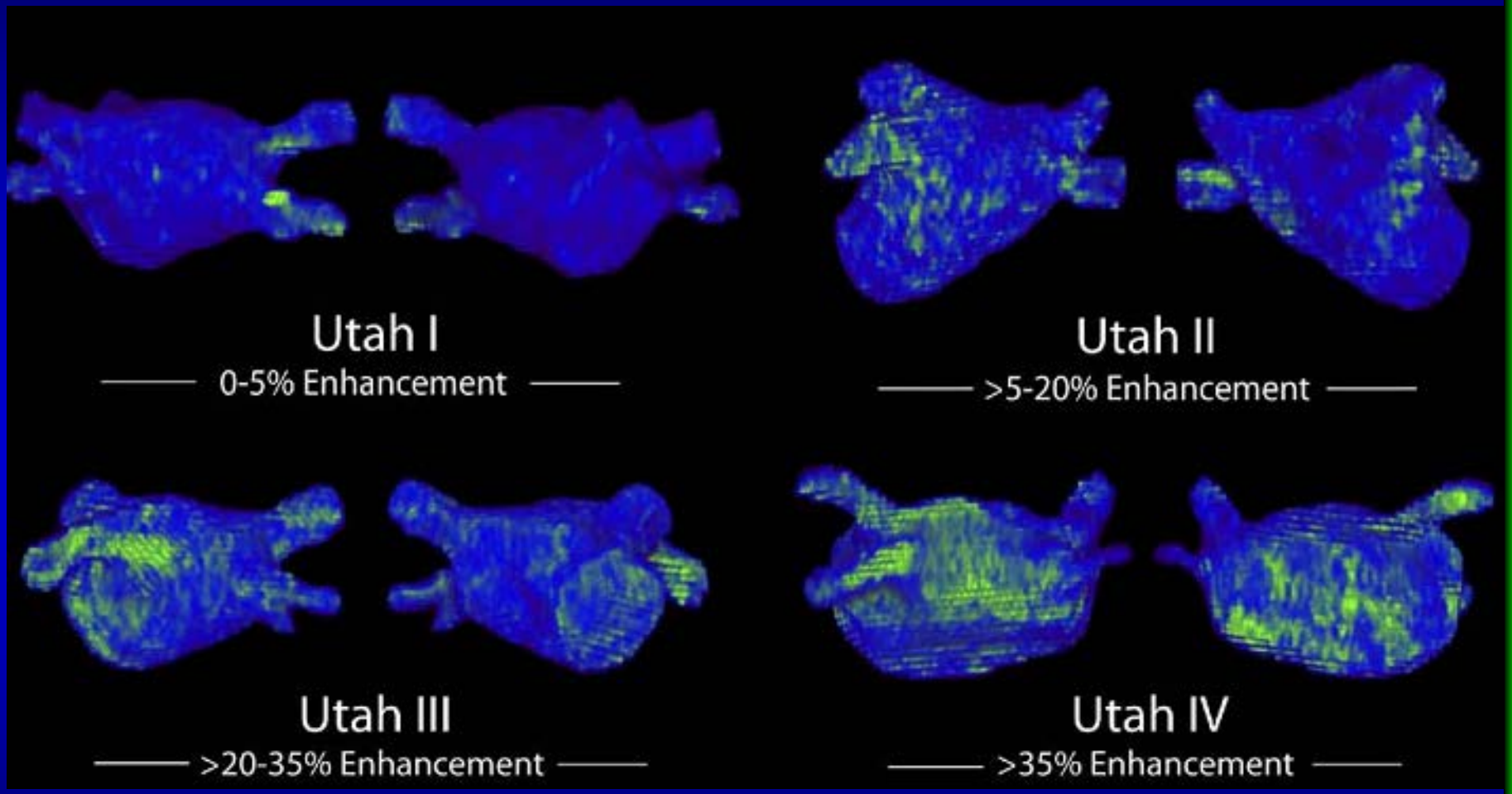
45 pts with idiopathic PAF

Follow-up: 8±6 months



Haissaguerre N Engl J Med 1998

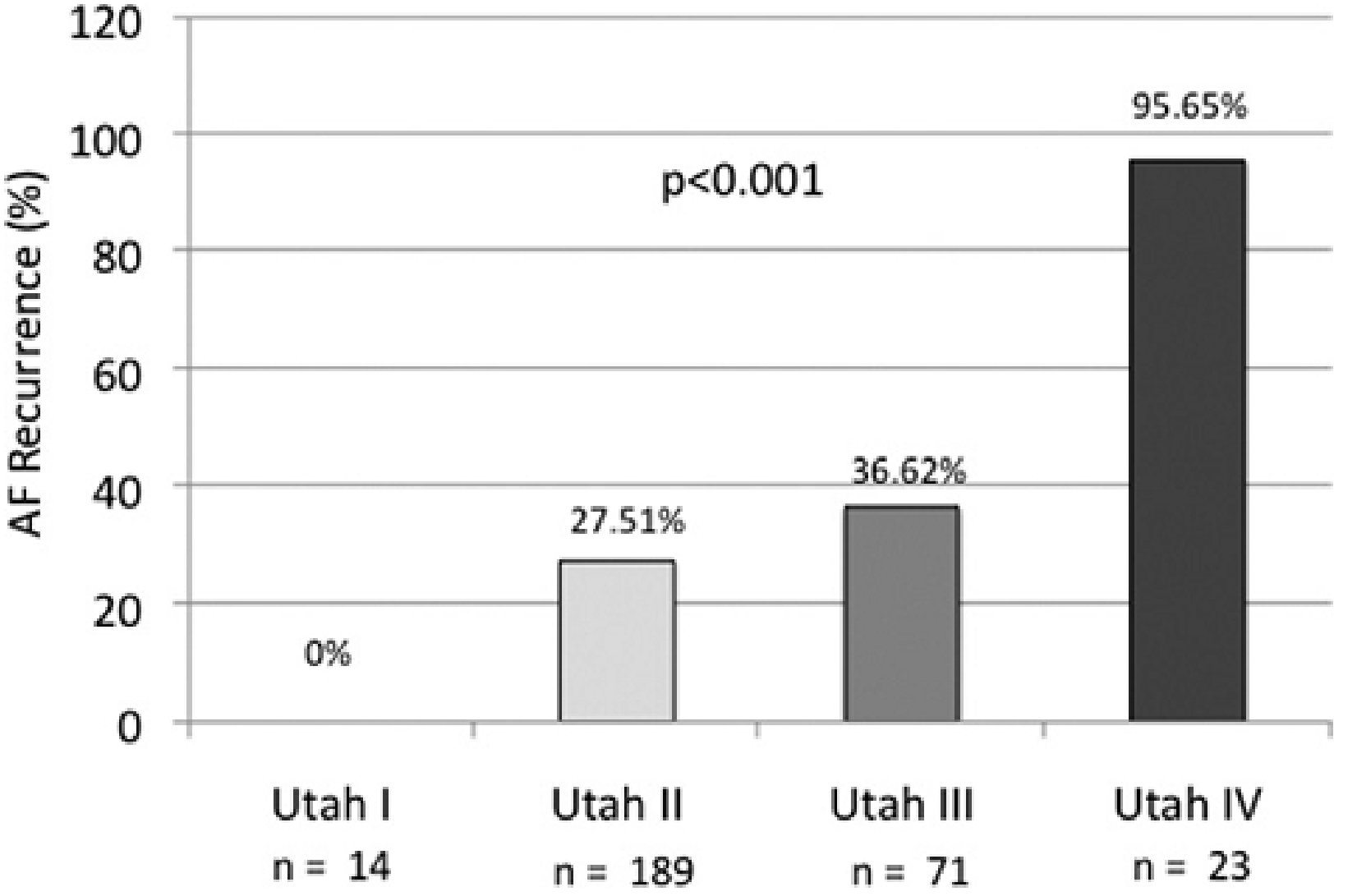
Structural substrate: fibrosis in vivo



333 patients evaluated by cardiac MR before AF ablation

Mahnkopf Heart rhythm 2010

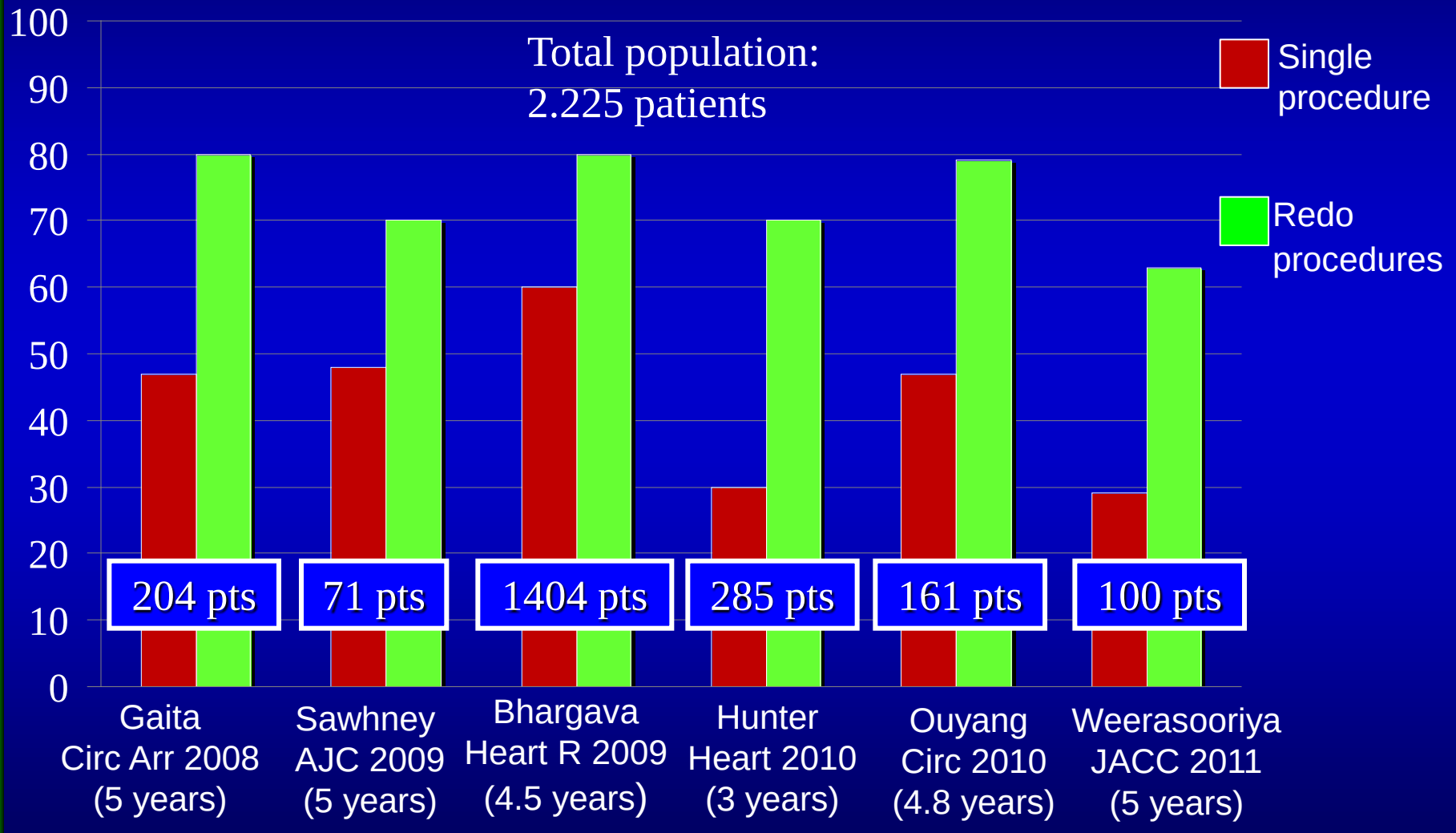
Structural substrate: fibrosis in vivo



Mahnkopf Heart rhythm 2010

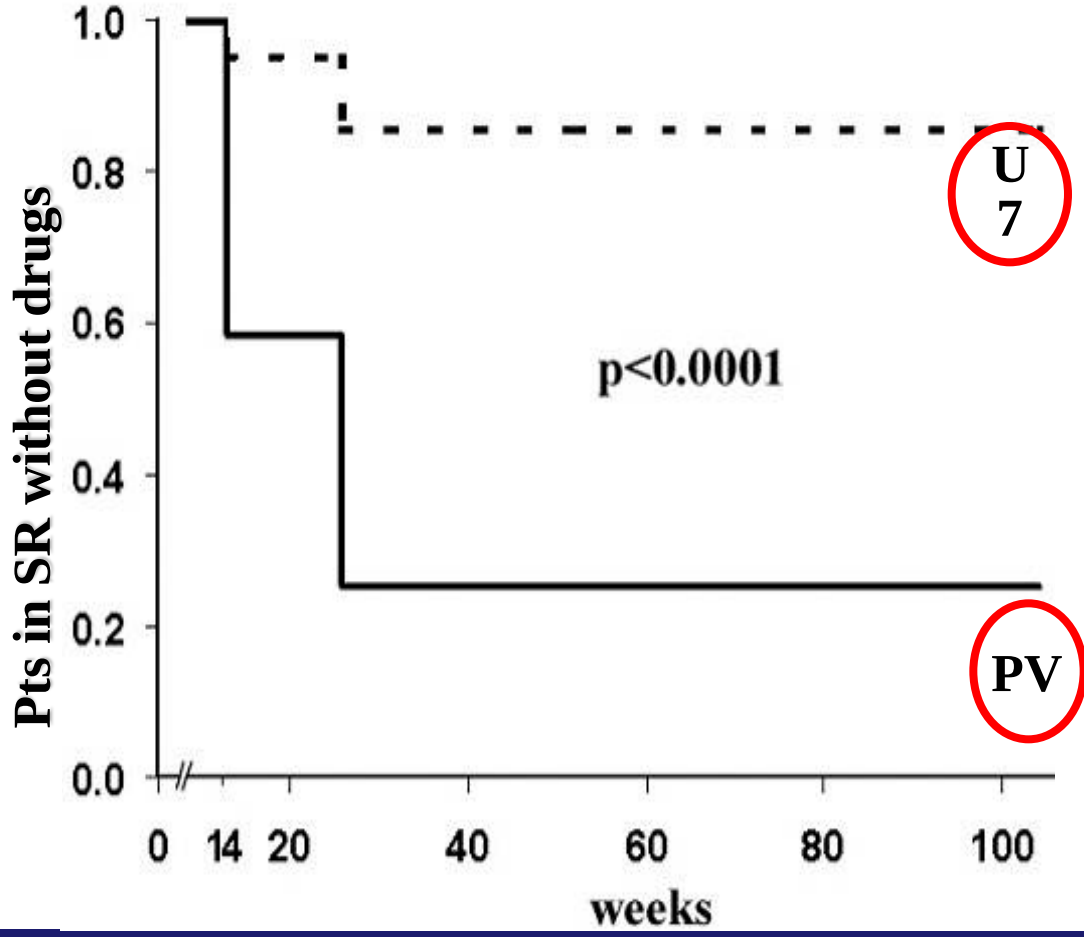
AF ablation outcome: long-term efficacy

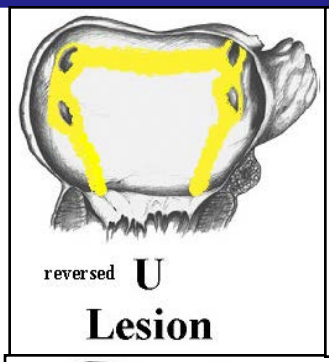
based on documented AF episodes lasting more than 30 secs

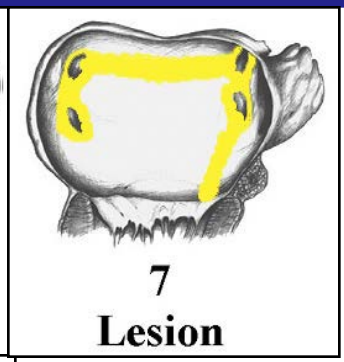


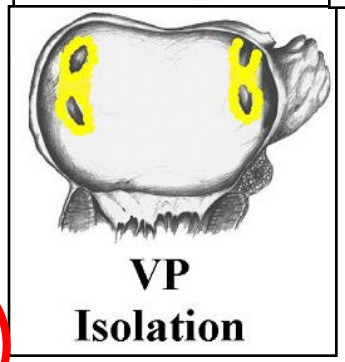
AF ablation in structural heart disease

Permanent AF and Valvular Heart Disease









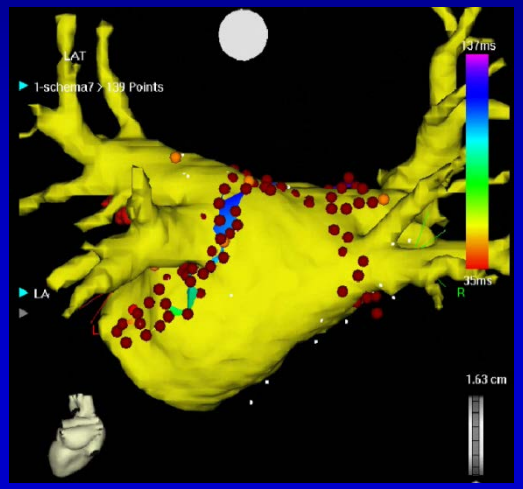
PV

Gaita Circulation 2005

AF ablation in structural heart disease: HCM

Total population : 78 pts

Success	Variable	HCM (n = 26)	Other cardiopathies (n = 26)	idiopathic (n = 26)
	Total	64%	65%	77%



Mean F-up

34±16 months

Major complications: none

Gaita Am J Cardiol 2007

AF ablation in structural heart disease: HF

Single Procedure (28%-55%)

Redo-Procedure ± AAD (63%-86%)

Complications (0%-5%)