Risk factor management to reduce the burden of AF

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SOUTH AUSTRALIA

SAHMRI South Australian Health & Medical Research Institute

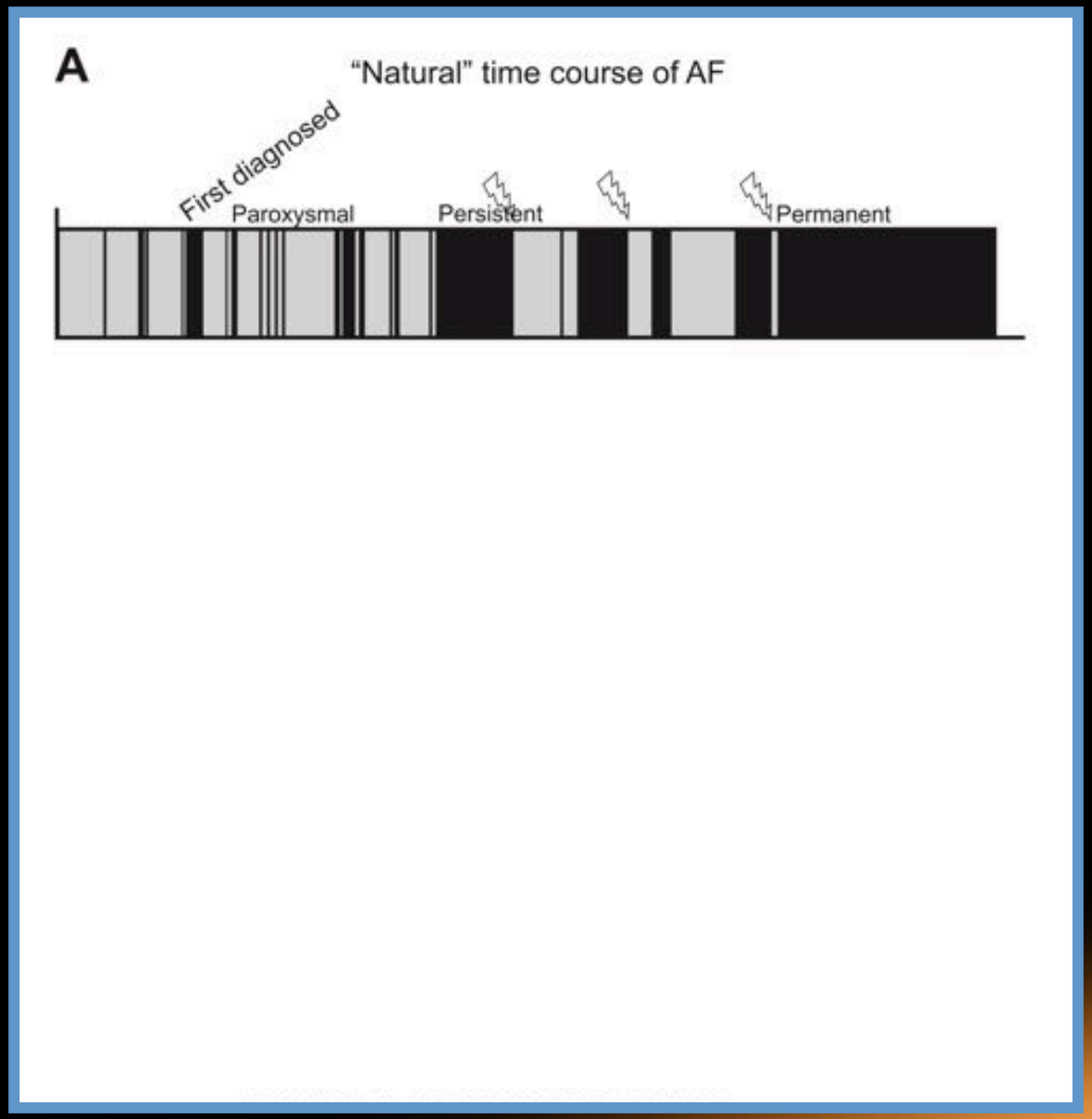
HEART HEALTH Centre for Heart Rhythm Disorders

THE UNIVERSITY of ADELAIDE

Disclosures 2015

- **Advisory Board:** Biosense-Webster, Medtronic, St Jude Medical
- **Lecture Fees and Research Funding:** Biosense-Webster, Medtronic, Boston Scientific, Biotronik, Sorin and St Jude Medical

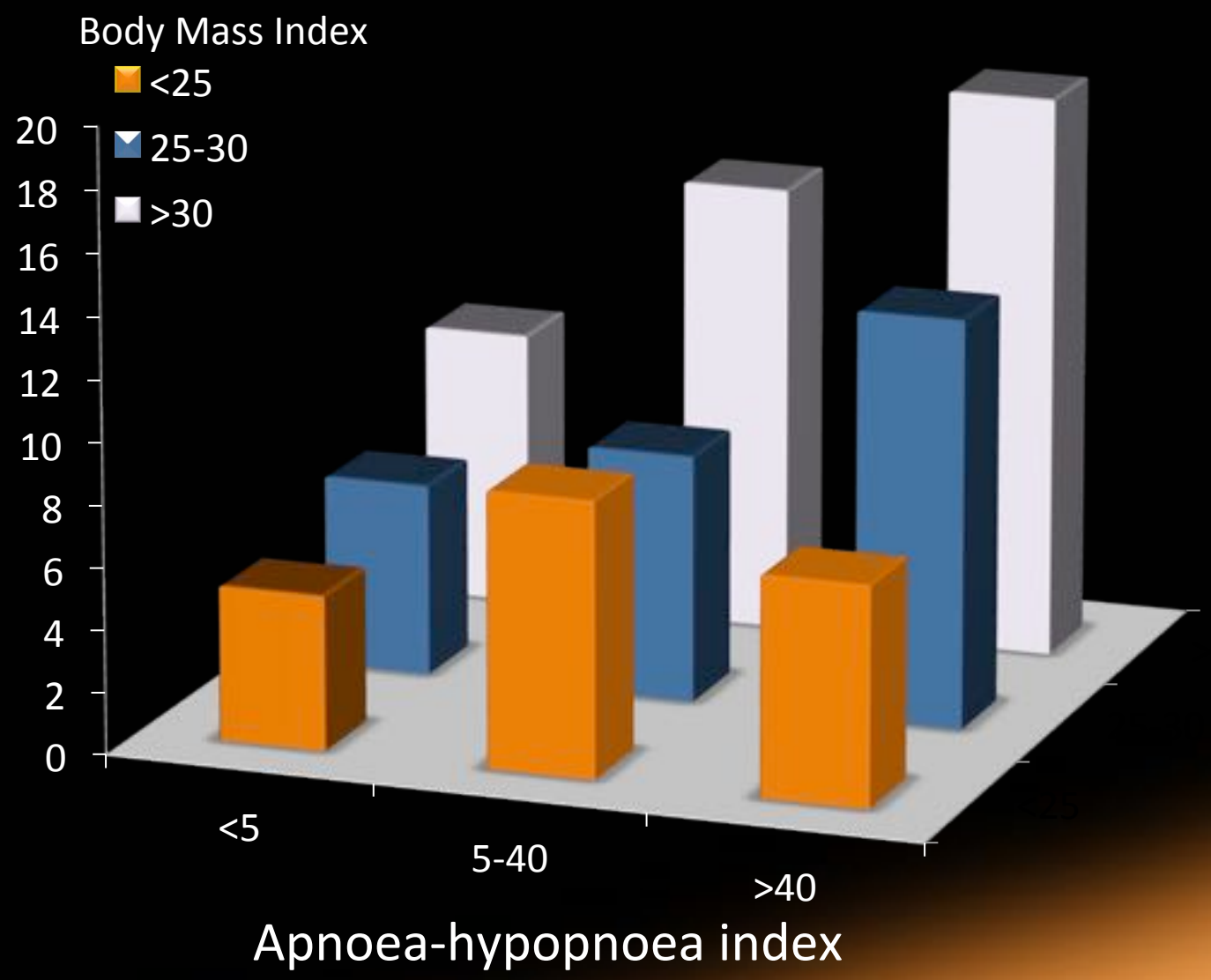
AF: Progressive Disease



Schotten et al – Physiol Rev 2011

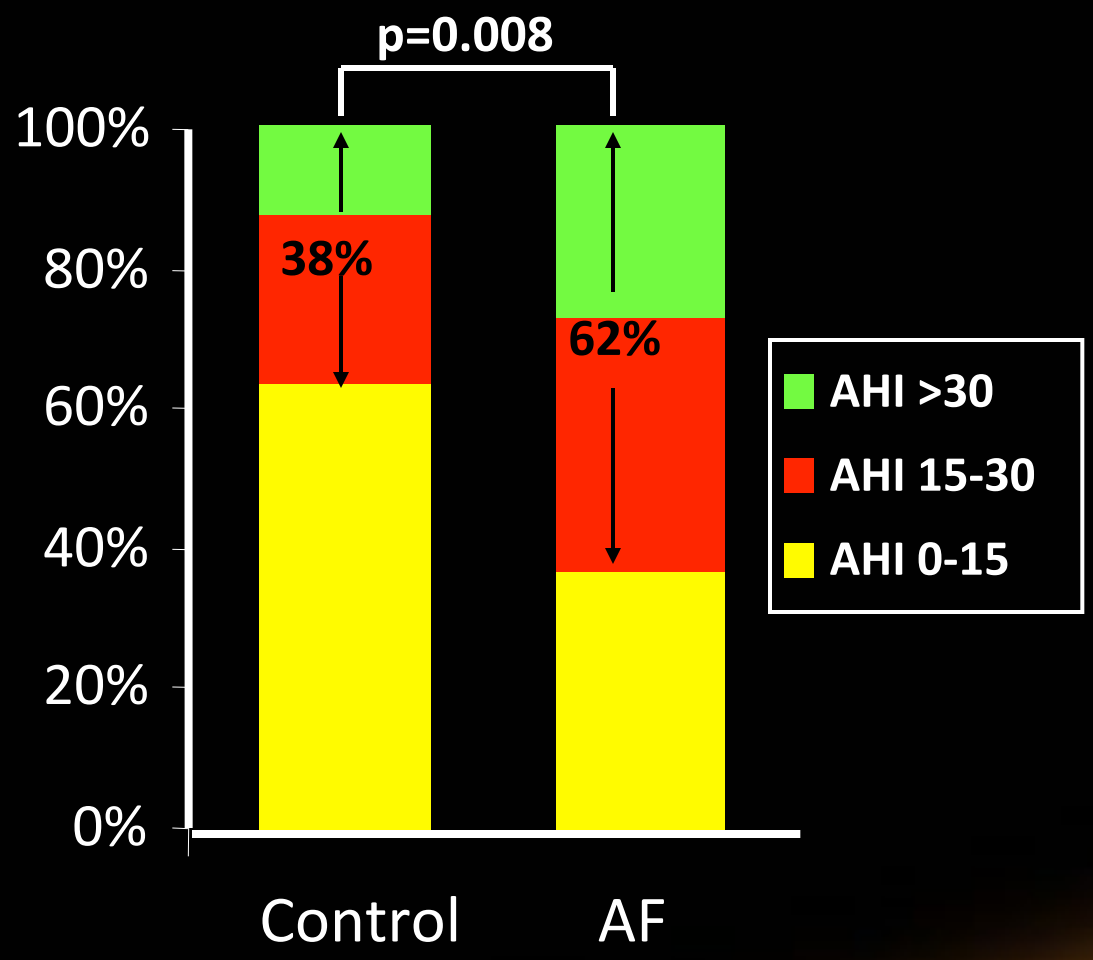
Known Risk Factors for AF
Aging
Hypertension
Heart Failure
Diabetes
Valvular Heart Disease
Ischemic Heart Disease
Congenital Heart Disease
Infiltrative Heart Disease
Obesity
Sleep Apnea
Pre-HT & Aortic Stiffness
Familial AF

Obesity, Sleep Apnea and AF



Gami et al, JACC 2007

Sleep disorderd breathing prevalence AF vs. controls

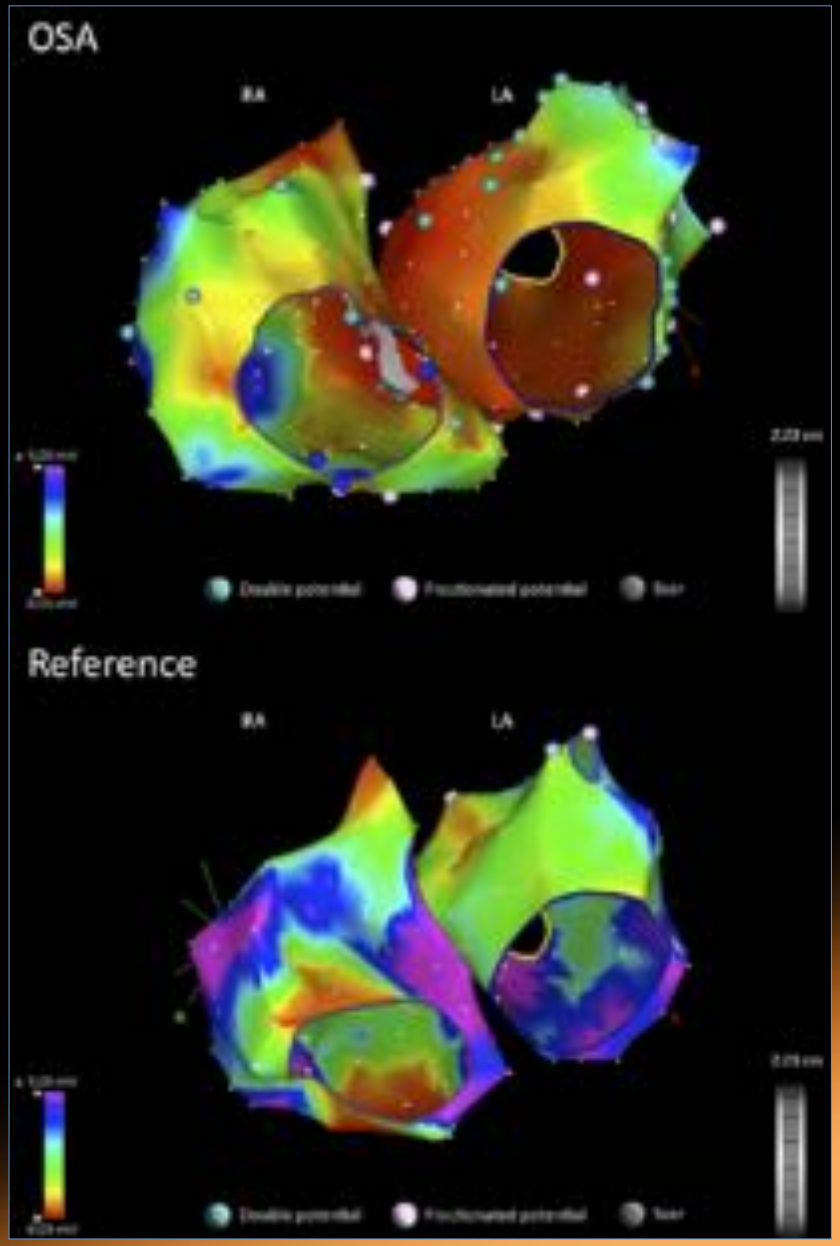


Moderate-Severe SDB (AHI>15)	
AF	62%
Controls	38%
P value	0.008

Stevenson et al EHJ 2008

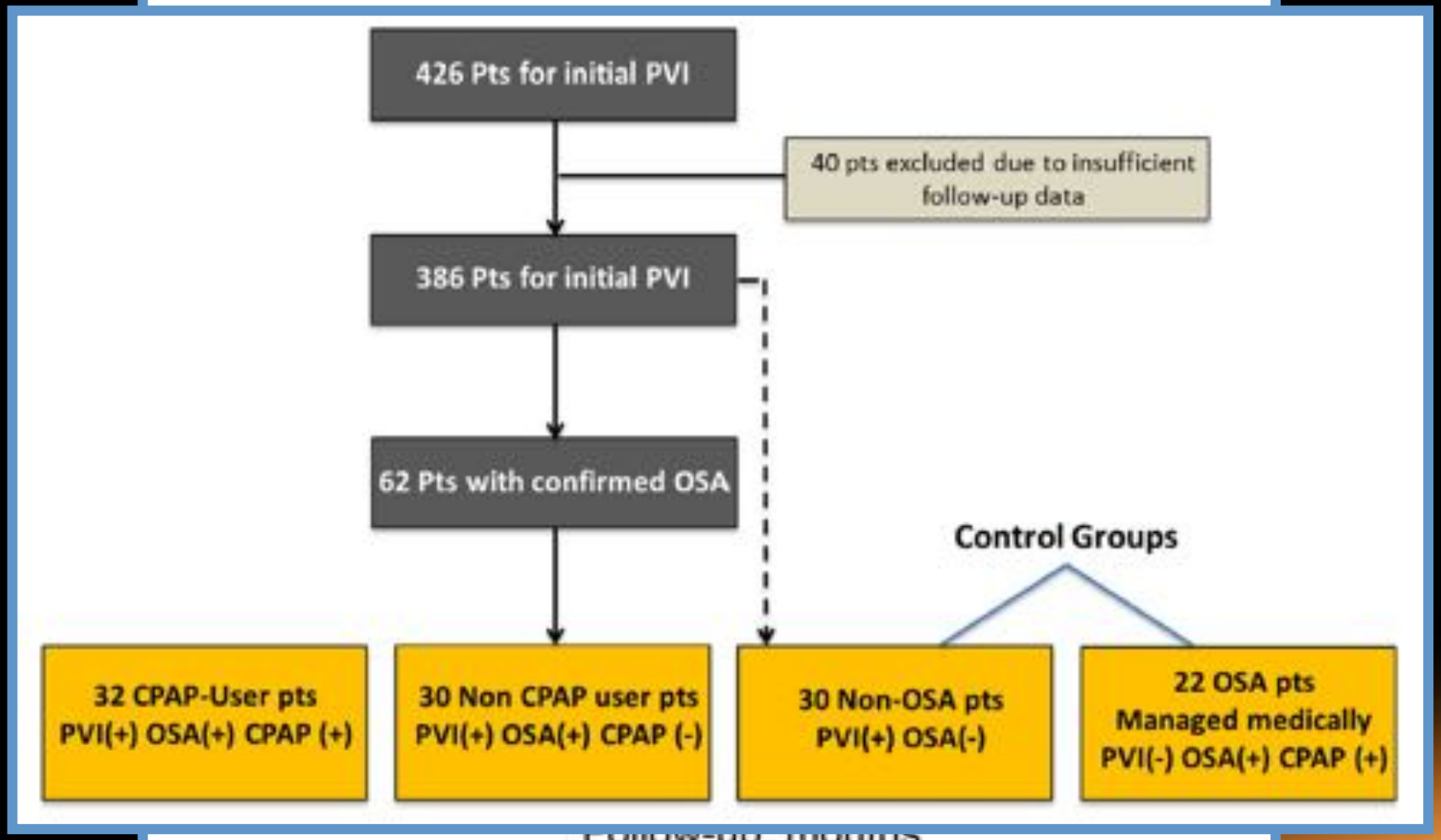
Chronic atrial remodeling due to OSA

	Reference (n = 20)	OSA (n = 20)	P
Males	16	17	1
Age (y)	51 ± 12	55 ± 12	.5
BMI	29 ± 3.5	32 ± 7.0	.2
Neck circumference	41 ± 4	42 ± 5	.5
Hypertension (treated)	9	11	.7
Structural heart disease	0	0	1
AFSS			.3
Duration	7 (6–9)	8 (7–8)	
Frequency	3 (4–5)	5 (3–7)	.07
Echocardiography data			
LA area indexed BSA (cm^2/m^2)	9.2 ± 1.3	13 ± 3.8	.009
E/e'	9.2 ± 1.1	9.6 ± 1.1	.8
Estimated RV systolic pressure	17.9 ± 3.4	19.6 ± 4.2	.2
IVSd (cm)	1.09 ± 0.1	1.15 ± 0.1	.3
LVPWd (cm)	1.1 ± 0.07	1.1 ± 0.13	.3
LVEDD (cm)	5.2 ± 0.2	5.3 ± 0.1	.8
LVESD (cm)	3.1 ± 0.4	3.3 ± 0.7	.4
LVEF (%)	62 ± 1	60 ± 1	.7
Polysomnography data			
Sleep efficiency (%)	78 ± 3	80 ± 2	.6
Mean AHI	6 ± 3	38 ± 22	<.0001
Mean CAI	1 ± 1.2	2.6 ± 2.5	.09
Desaturations ≥3%/h (no.)	7 ± 3	25 ± 14	<.0001
Epworth sleepiness scale	7 (4–9)	7 (5–9)	1



Dimitri H et al. Heart Rhythm 2012

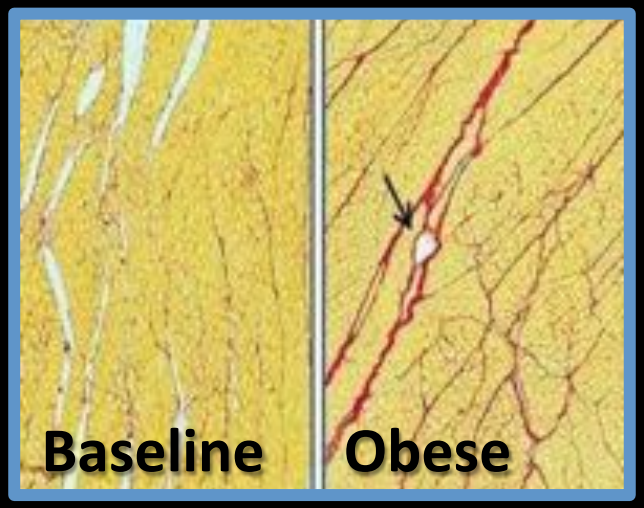
OSA treatment & AF Recurrence



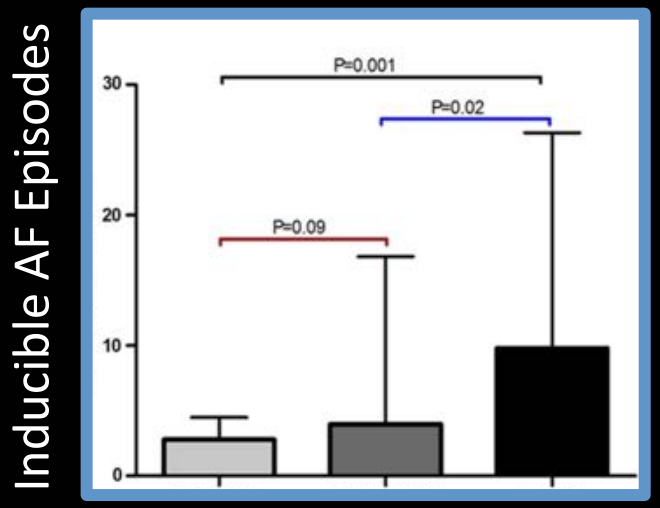
Fein et al. JACC 2013

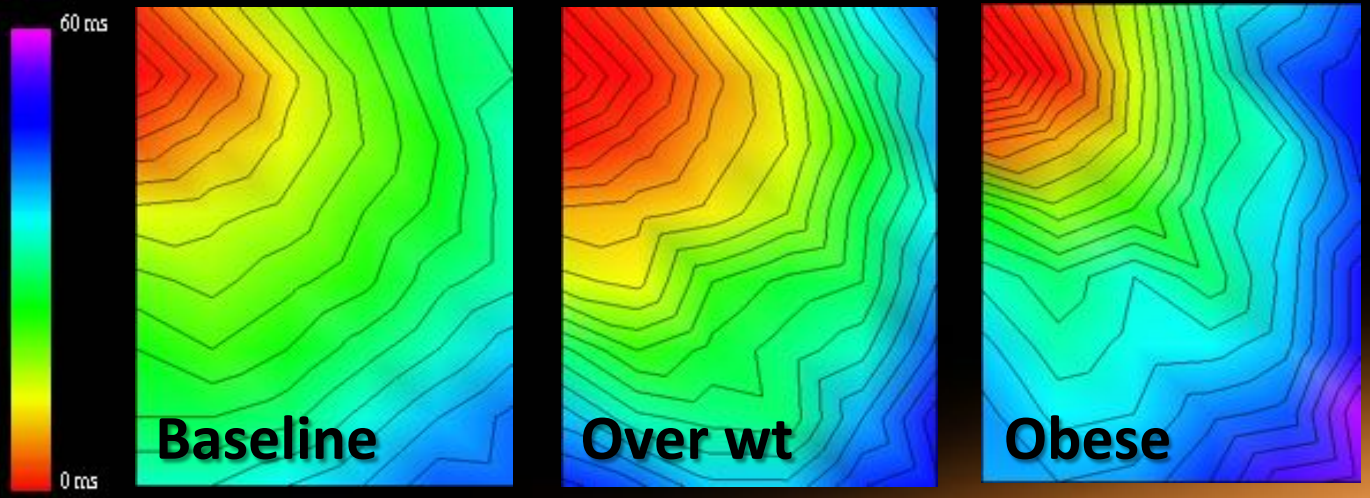
Atrial substrate due to weight gain

Atrial Fibrosis



AF Inducibility



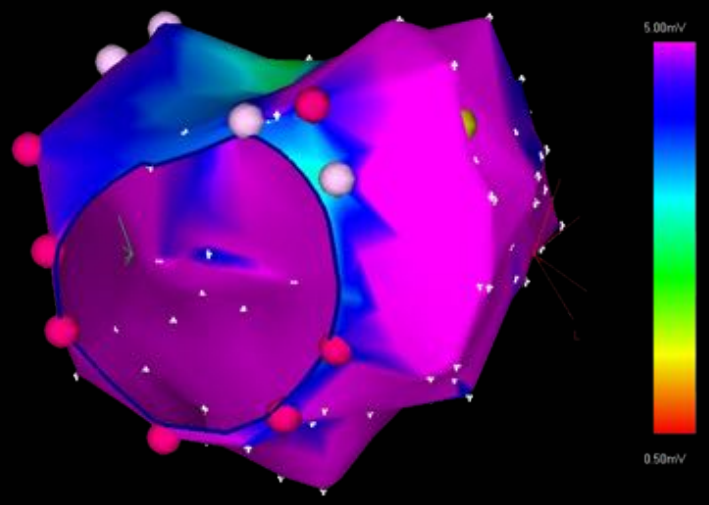


Abed et al, Heart Rhythm 2013

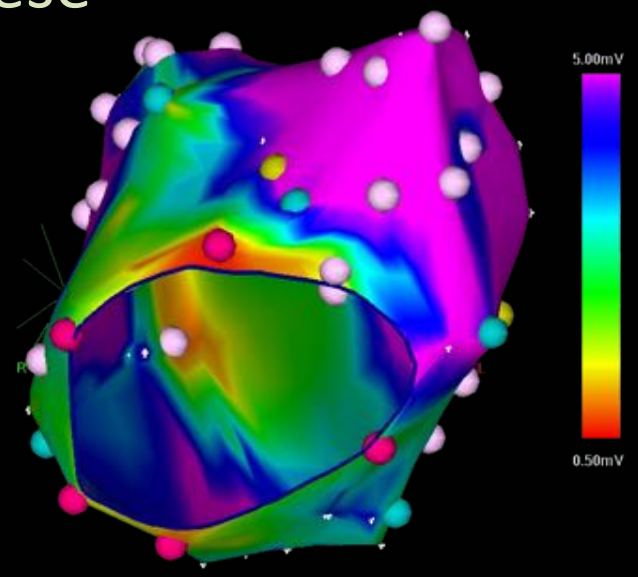
Fatty infiltration of posterior LA: a new substrate for AF

Mahajan R et al, JACC 2015

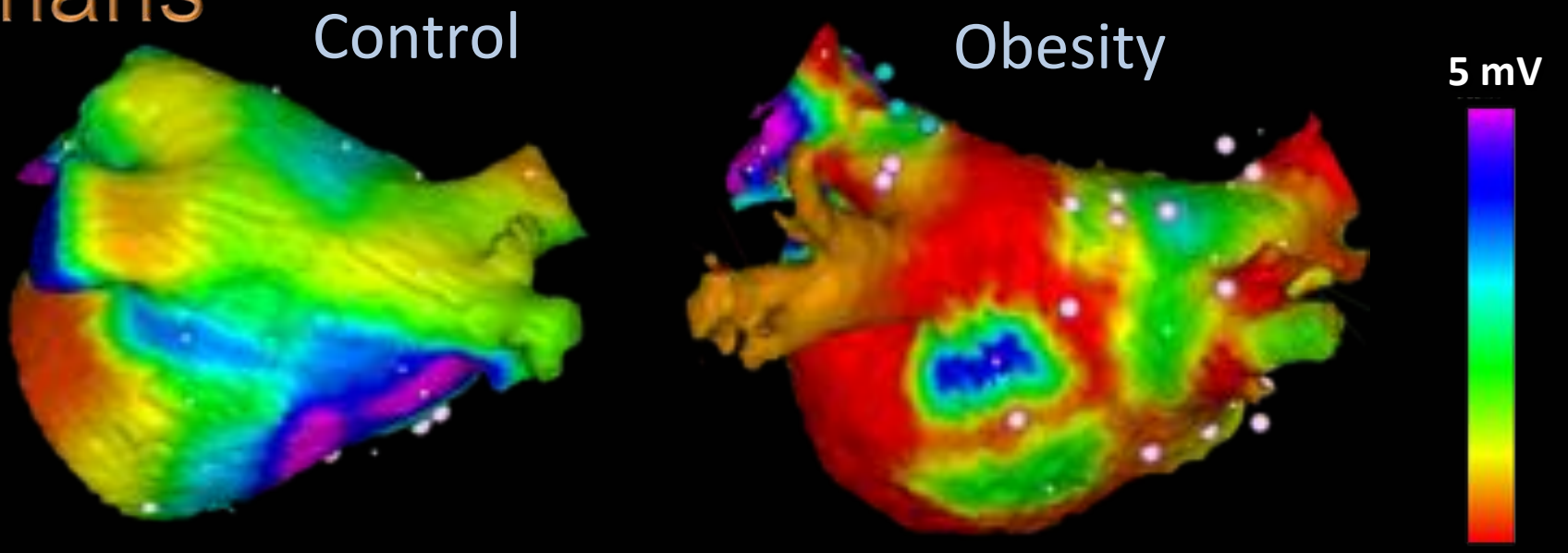
Control

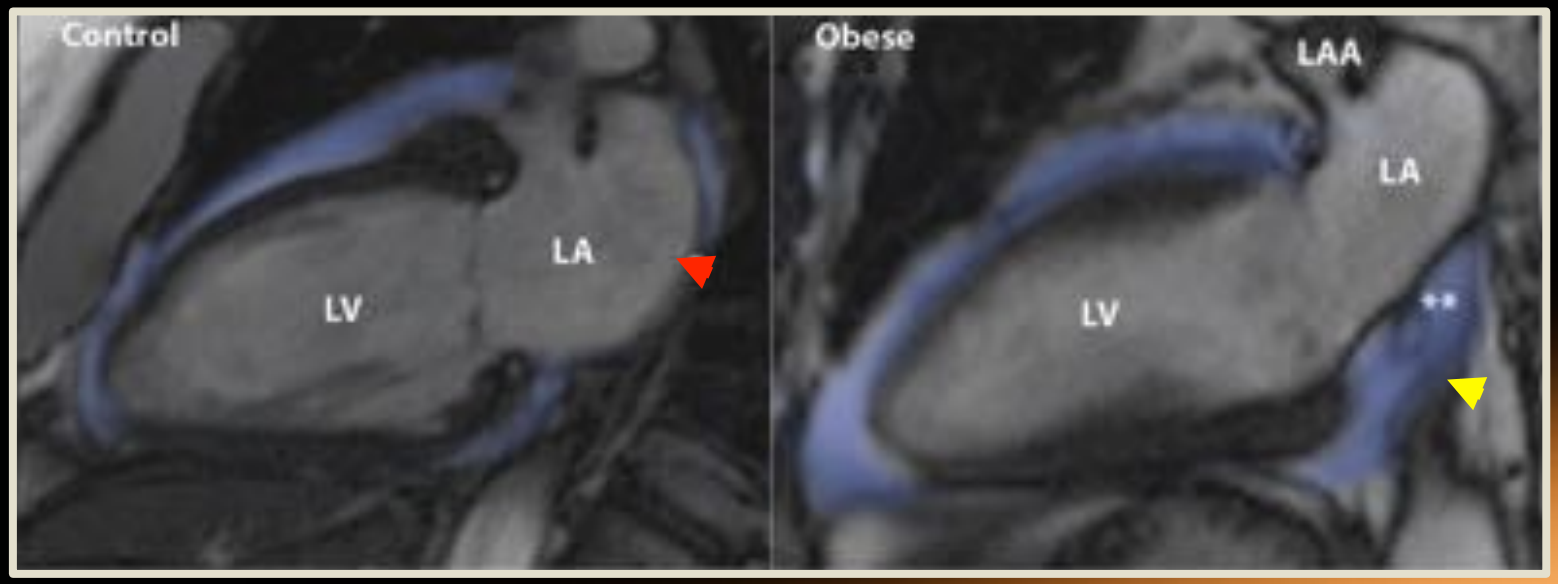


Obese



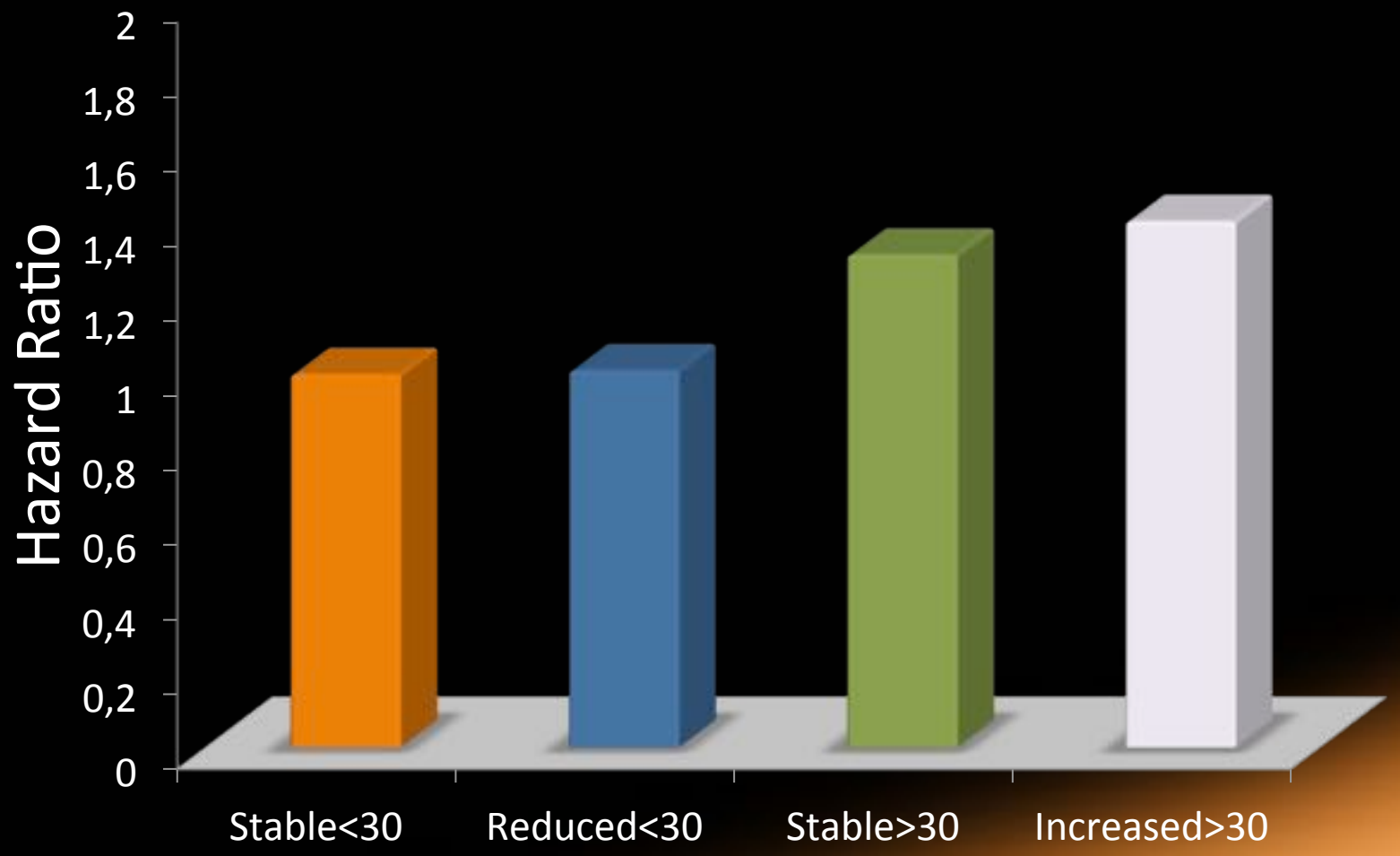
Atrial remodeling due to obesity in humans





Mahajan R et al, Prystowsky Clinical Research Award HRS 2015

Weight Change and AF Risk



WHS JACC 2010

Impact of weight reduction

30 Obese Sheep (72 weeks)

High Calorie dense diet

Stable Obese
High calorie-dense feeding

16 wk

15% Weight Reduction
Diet restriction

16-32 wk

30% Weight Reduction
Diet restriction

32 wk

Maintenance diet

8 Lean Control Sheep

Control arm
Maintenance diet

32 wk

Investigations

- DEXA Scan
- Cardiac MRI
- Epicardial EP Study
- Histology
- Immunohisto-chemistry
- Western blot

Mahajan et al, HRS YIA 2013

Hemodynamic and MRI Characteristics

	Lean control group	Obese group	15% Weight loss group	30% Weight loss group	p value	
					Obese vs Control	Obese vs 30% Weight loss
Weight (kg)	58±6	111±12	94±9	77±8	<0.001	<0.001
Total Body fat (kg)	7±4	40±9	31±4	20±8	<0.001	<0.001
LA pressure (mmHg)	3.8±1.5	9.3±2.0	6.5±3.5	5.3±2.9	<0.001	0.007
PA pressure (mmHg)	9.5±2.3	15.1±2.5	13.5±2.5	10.9±2.0	<0.001	0.002
LA (EDV) (ml)	29±2	-*	46±7	31±3	0.001**	0.003
LVEF (%)	52.5±5.3	-*	52.4±4.7	51±0.7	NS**, #	NS#

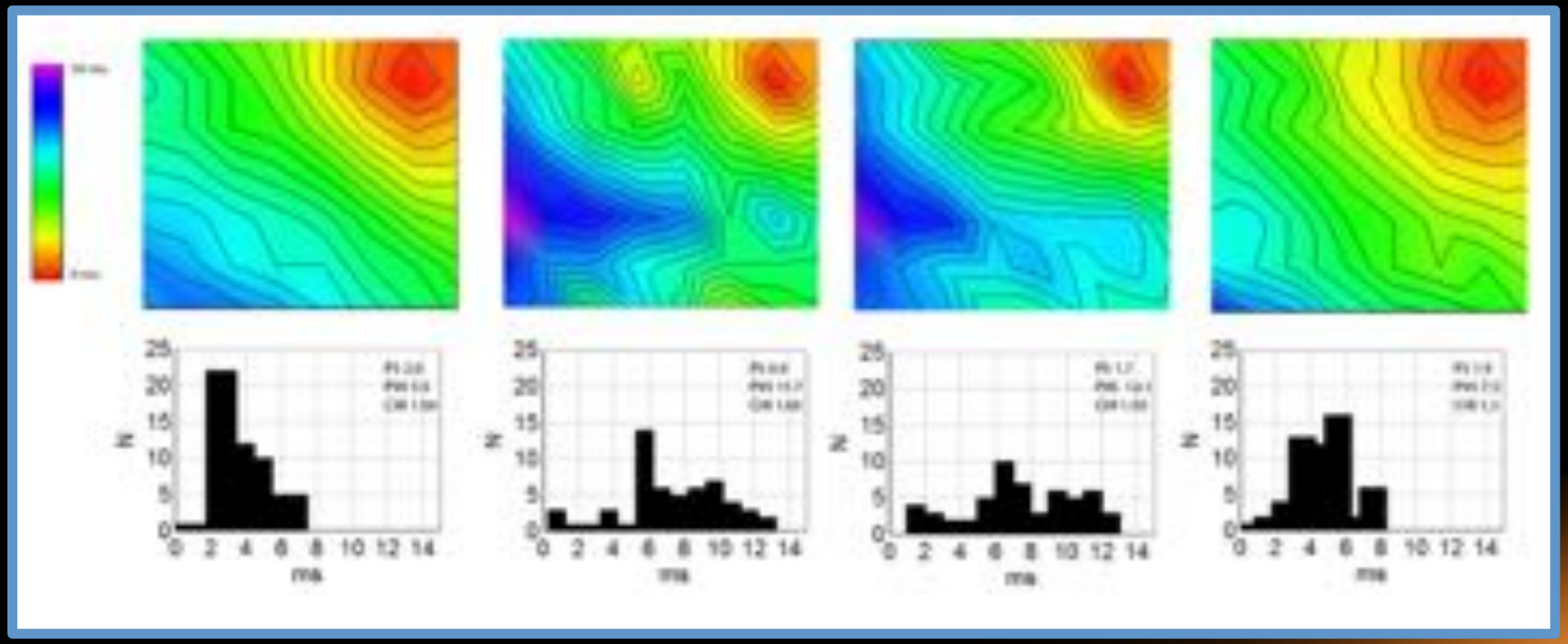
* - CMR not performed as sheep did not fit in scanner

** -p Value-15% vs 30% Weight loss

\# -group effect not significant

Conduction velocity and heterogeneity

Lean Control | Obese | 15% Weight Loss | 30% Weight Loss

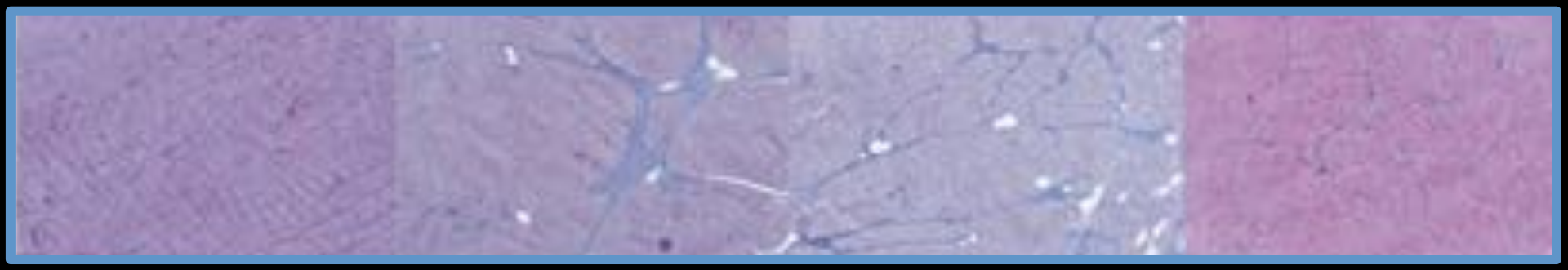


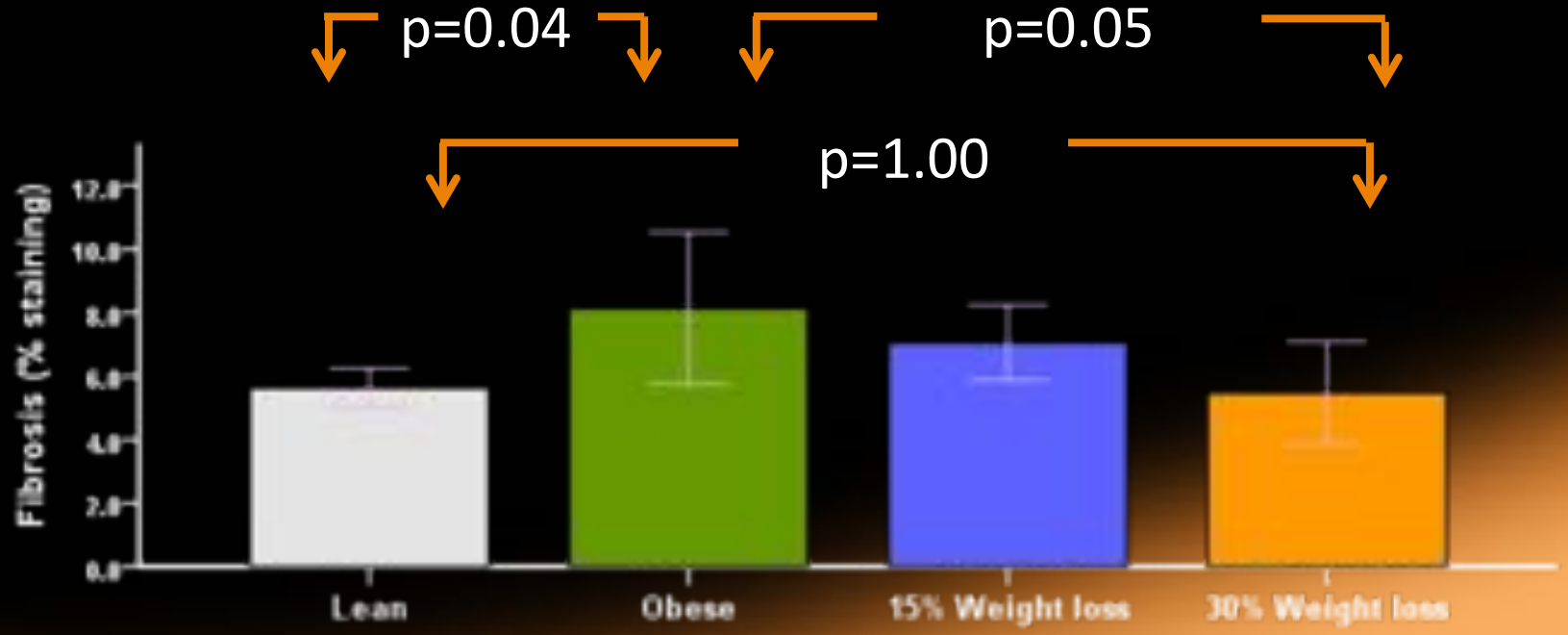
Mahajan et al, HRS YIA 2013

Atrial Fibrosis: Morphometric Analysis

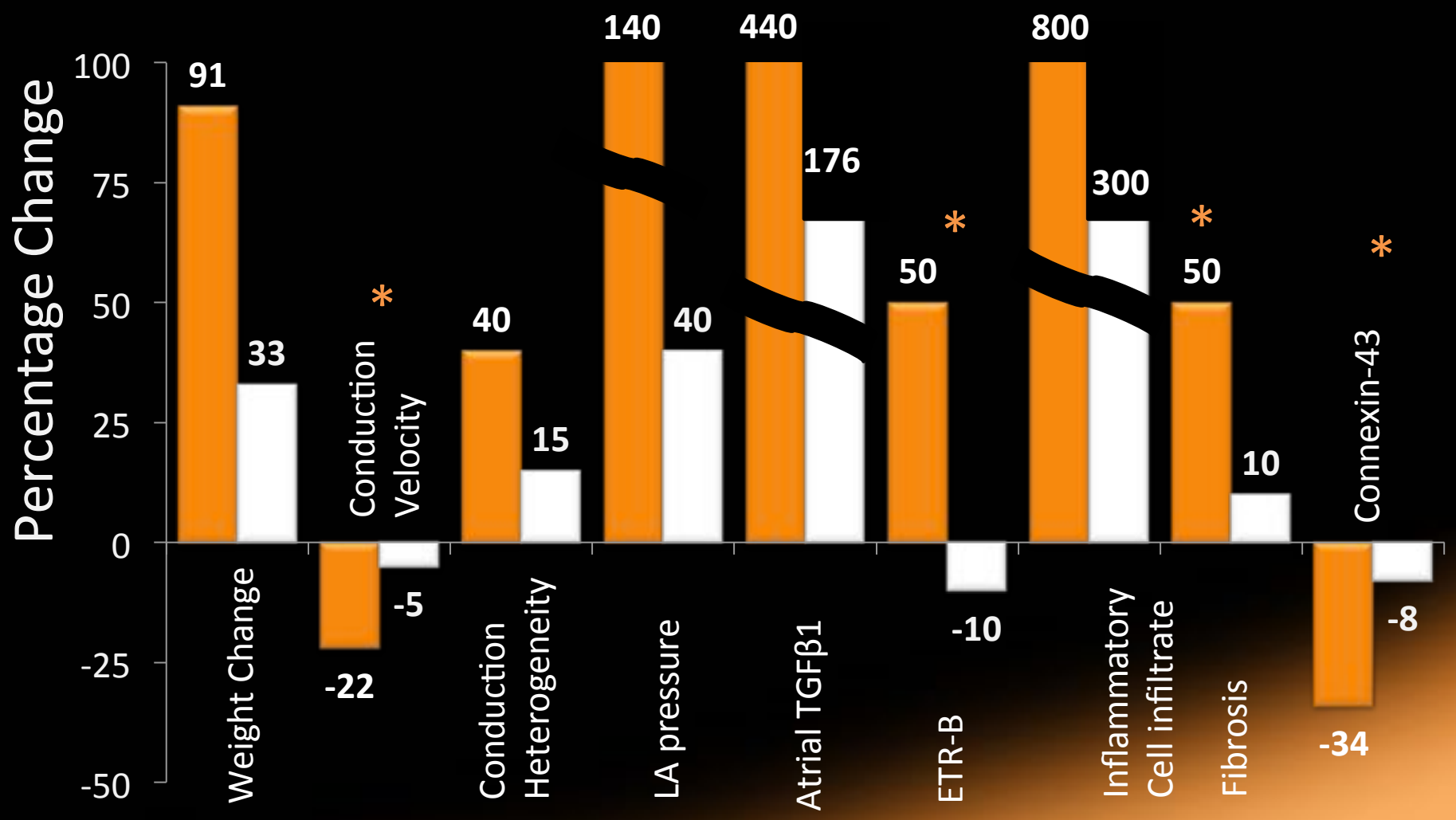
Masson's Trichrome

Lean Control | Obese | 15% Wt Loss | 30% Wt Loss





Dynamic change in AF substrate with weight gain and reduction



Original Investigation

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

A Randomized Clinical Trial

Hany S. Abed, BPharm, MBBS; Gary A. Wittert, MBBch, MD; Darryl P. Leong, MBBS, MPH, PhD; Masoumeh G. Shirazi, MD; Bobak Bahrami, MBBS; Melissa E. Middeldorp; Michelle F. Lorimer, BSc; Dennis H. Lau, MBBS, PhD; Nicholas A. Antic, MBBS, PhD; Anthony G. Brooks, PhD; Walter P. Abhayaratna, MBBS, PhD; Jonathan M. Kalman, MBBS, PhD; Prashanthan Sanders, MBBS, PhD

JAMA 2013

248 highly symptomatic AF patients with BMI>27 & WC >100 (male) or >90 (female)

Exclusions: Serious medical/psychiatric disorder; Recent weight loss program; Malabsorption disorder; Unstable INR; LVEF≤35%; DM – on insulin; Valvular disease; Endocrinopthy

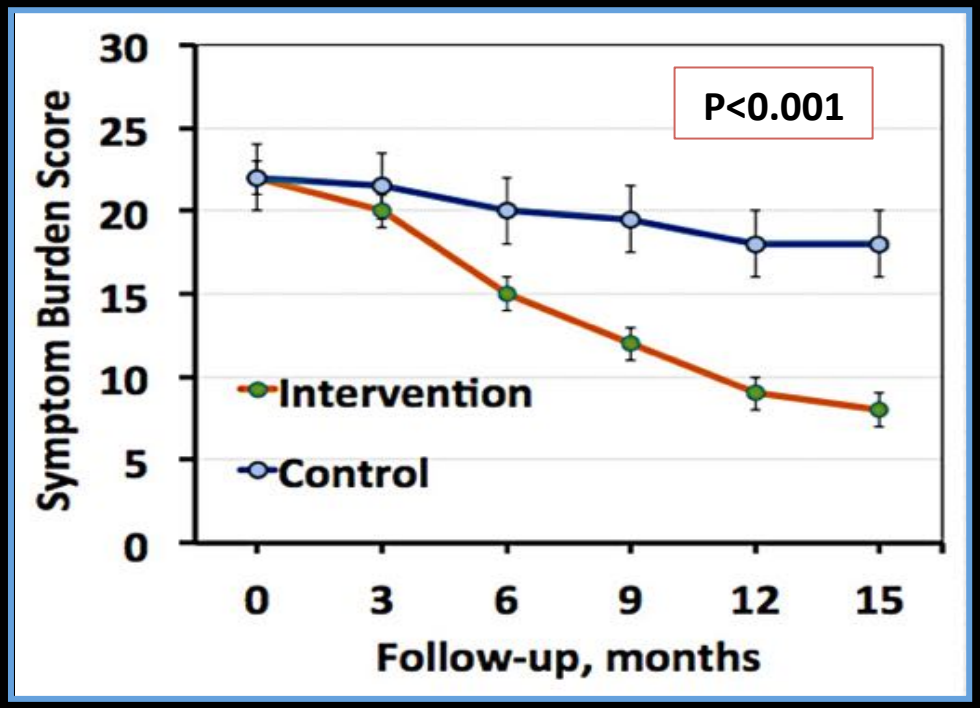
150 Randomised

75 Control

75 Intervention

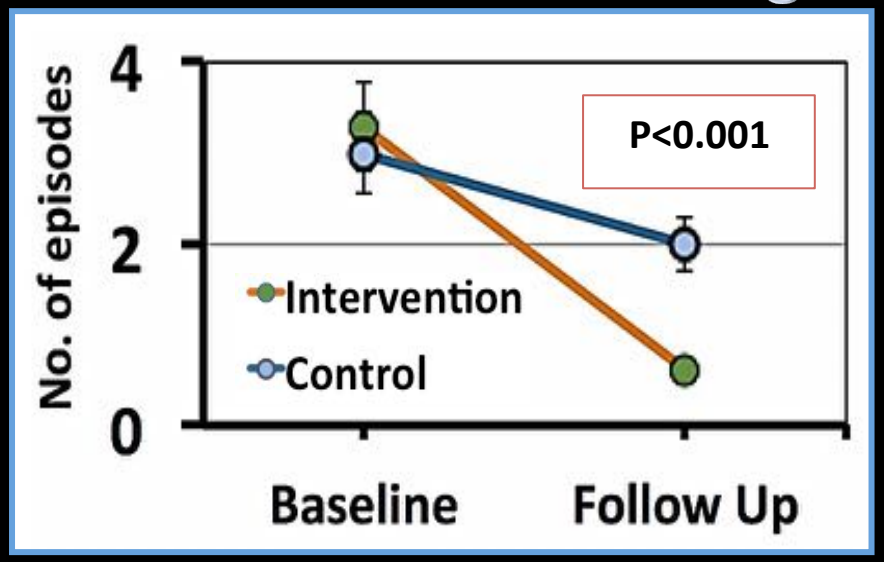
Effect of short-term weight loss

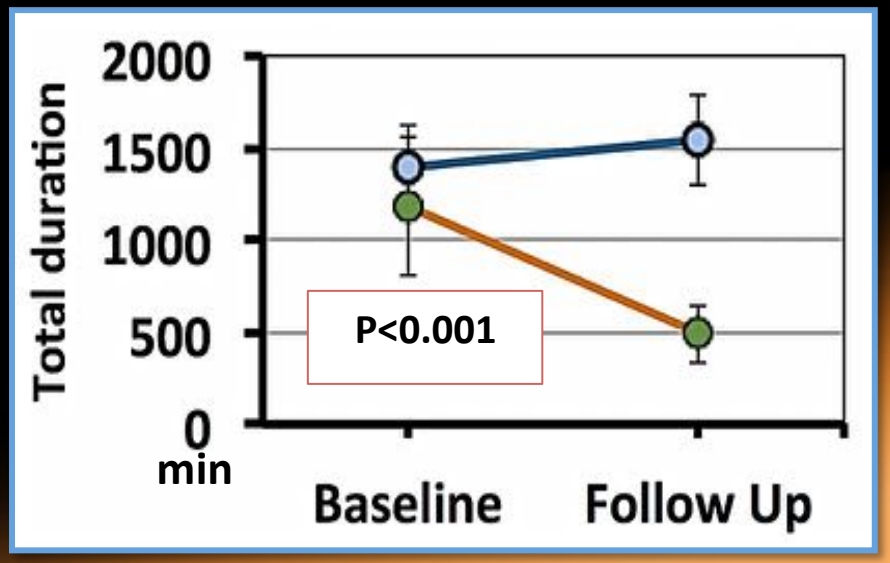
Symptom Burden Score



Abed et al. JAMA 2013

Continuous Monitoring





Long-Term Effect of Goal-Directed Weight Management in an Atrial Fibrillation Cohort

A Long-Term Follow-Up Study (LEGACY)

Rajeev K. Pathak, MBBS,* Melissa E. Middeldorp,* Megan Meredith,* Abhinav B. Mehta, MAcrSr,†
Rajiv Mahajan, MD, PhD,* Christopher X. Wong, MBBS, PhD,*‡ Darragh Twomey, MBBS,* Adrian D. Elliott, PhD,*§
Jonathan M. Kalman, MBBS, PhD,¶ Walter P. Abhayaratna, MBBS, PhD,# Dennis H. Lau, MBBS, PhD,*
Prashanthan Sanders, MBBS, PhD*

JACC 2015

Patients with BMI ≥ 27
N=825

↓

Weight Management

↓

Final Cohort
N=355

10%WL
N=135

3-9%WL
N=103

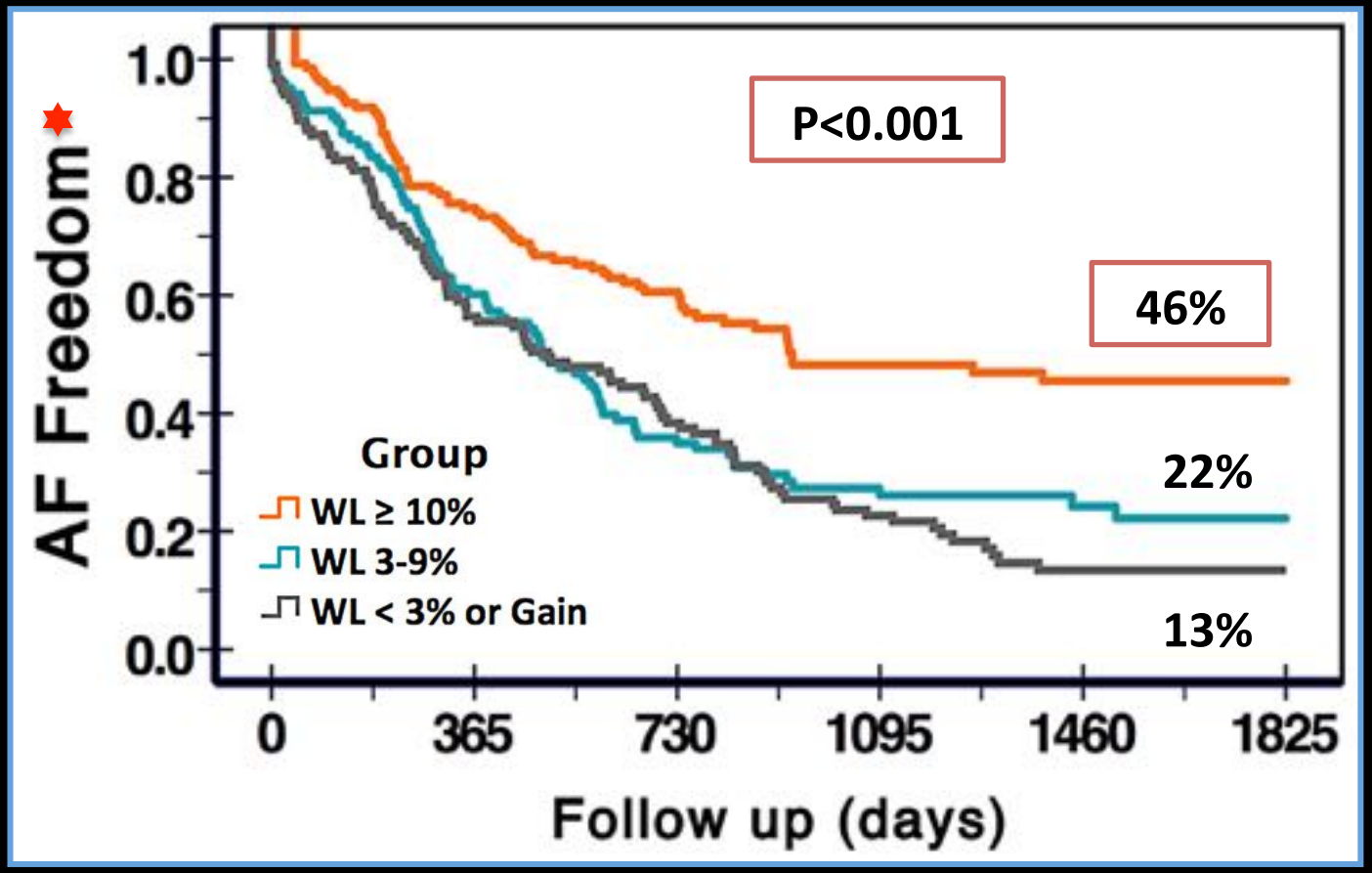
<3%WL or WG
N=117

Met Exclusion Criteria (N=293)
Terminal Cancer (N=10)
Inflammatory Dx (N=20)
Permanent AF (N=84)
AV Node ablation (N=12)
AF ablation (N=90)
Severe Medical Illness (N=77)

Patients from other States (N=177)

AF Freedom: drug & ablation-free

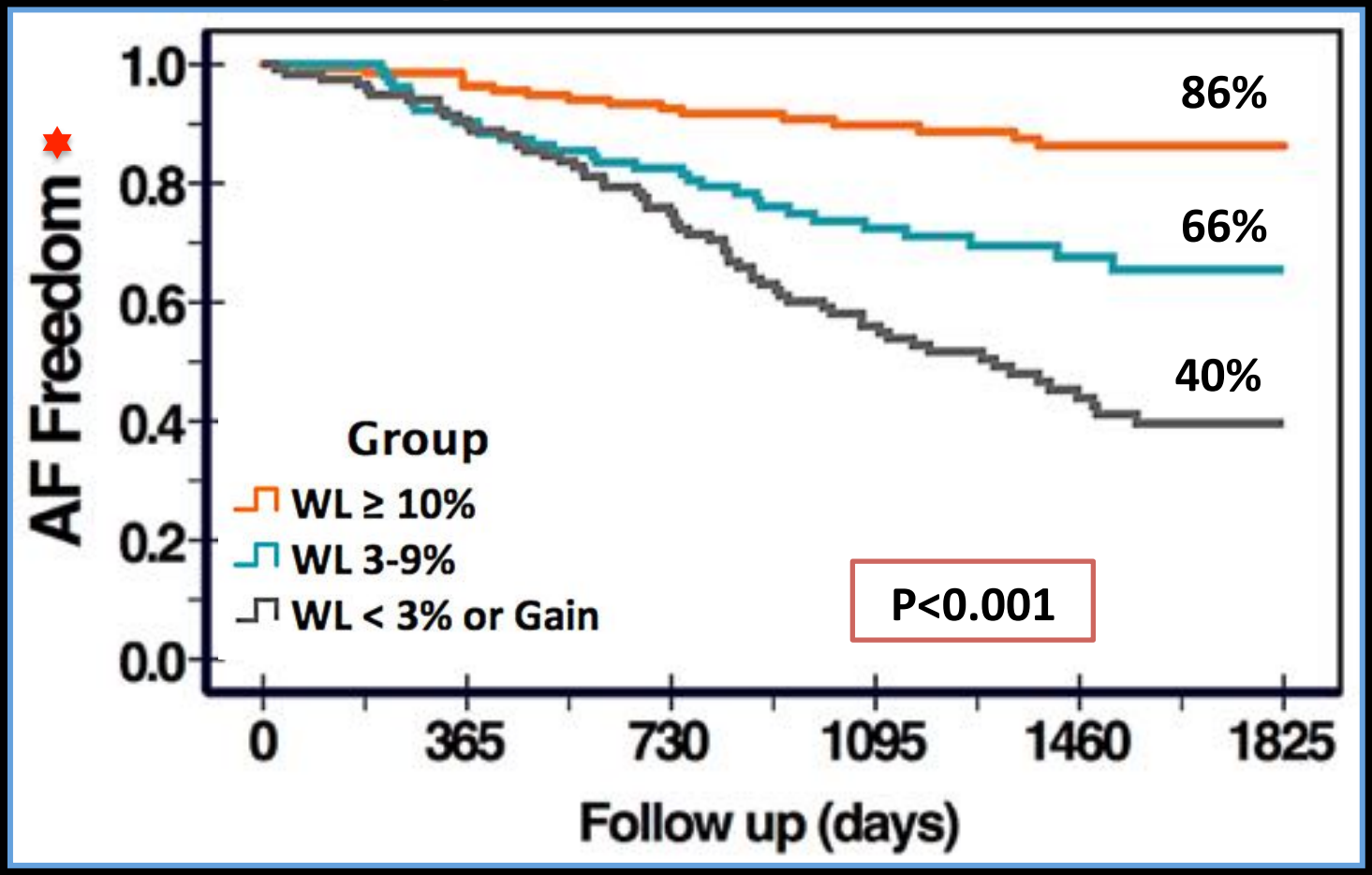
✱ Without AAD or ablation



Days	0	365	730	1095	1460	1825
≥10%WL	135	101	72	42	31	18
3-9% WL	103	62	36	22	13	7
<3% WL	117	66	44	22	11	9

Pathak RK, et al. JACC 2015

Total arrhythmia-free survival



* With AAD +/- abln

Days	0	365	730	1095	1460	1825
≥10%WL	135	130	114	86	67	36
3-9% WL	103	93	83	57	35	22
<3% WL	117	105	85	53	32	22

Pathak RK, et al. JACC 2015

Impact of CARDIOrespiratory FITness on Arrhythmia Recurrence in Obese Individuals With Atrial Fibrillation

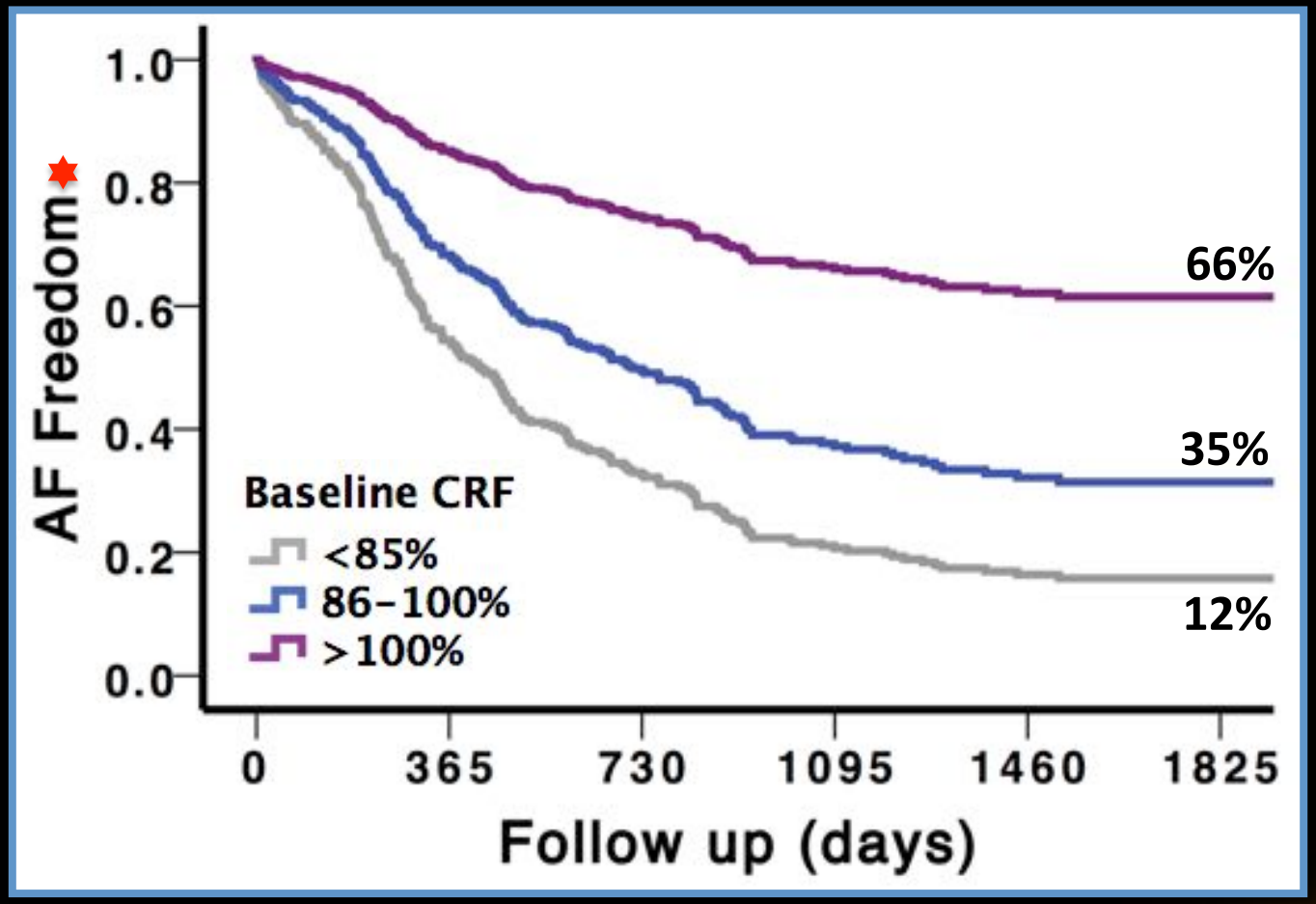
The CARDIO-FIT Study

Rajeev K. Pathak, MBBS,* Adrian Elliott, PhD,* Melissa E. Middeldorp,* Megan Meredith,*
Abhinav B. Mehta, M Acr Sr,† Rajiv Mahajan, MD, PhD,* Jeroen M.L. Hendriks, PhD,* Darragh Twomey, MBBS,*
Jonathan M. Kalman, MBBS, PhD,‡ Walter P. Abhayaratna, MBBS, PhD,§ Dennis H. Lau, MBBS, PhD,*
Prashanthan Sanders, MBBS, PhD*

JACC 2015

- **Structured: age and ability matched**
- **Frequency: three days to five days**
- **Intensity: Low to Moderate**
- **Time: 60 to 200 Minutes /Week**
- **Type : Aerobic & strength training**
- **Heart Rate: Monitor, 85% of 220-age**

AF Freedom: Drug & Ablation-Free

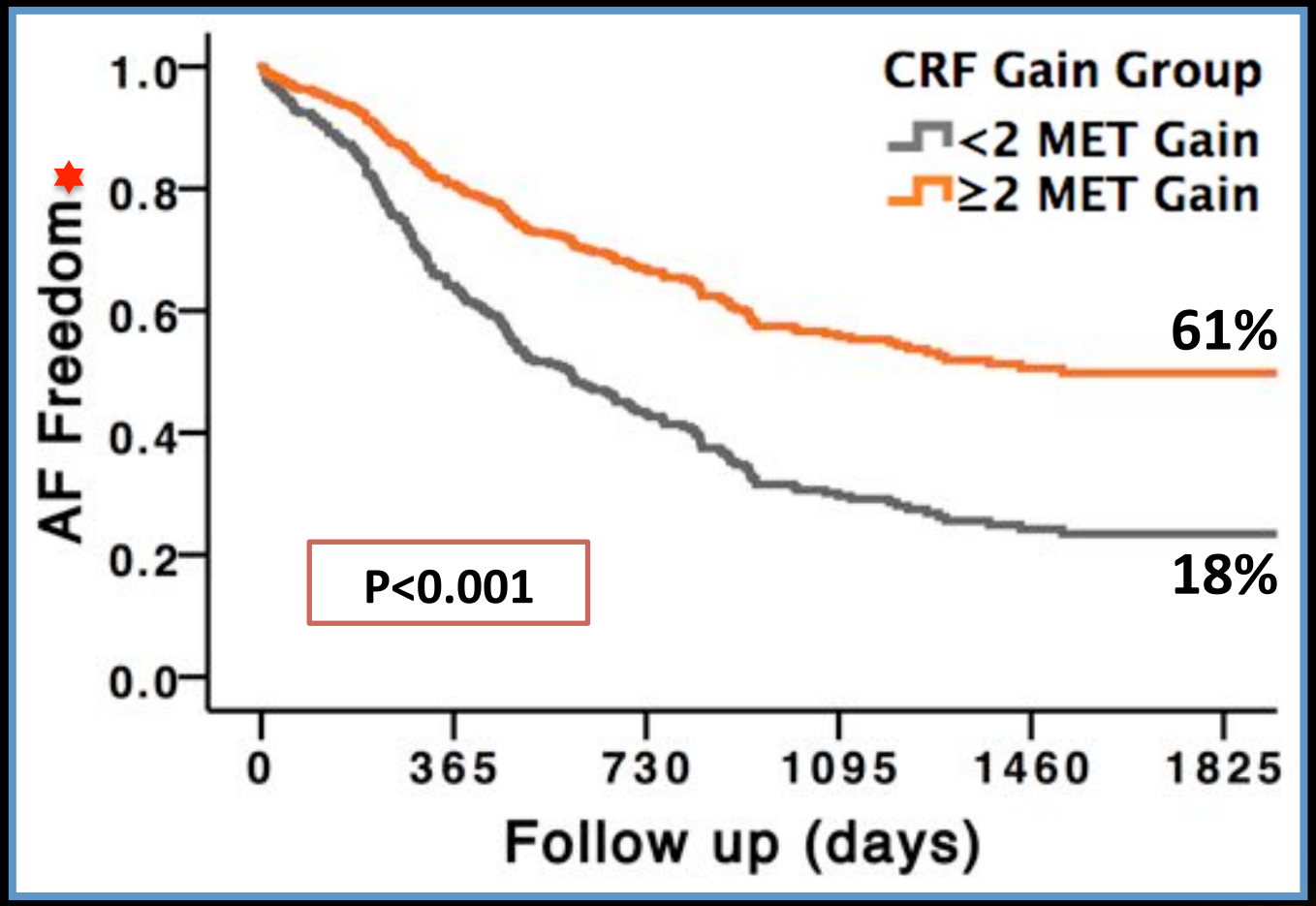


*Without AAD or ablation

Days	0	365	730	1095	1460	1825
<85%	95	54	36	16	12	6
86-100%	134	93	56	34	19	11
>100%	79	63	50	36	26	18

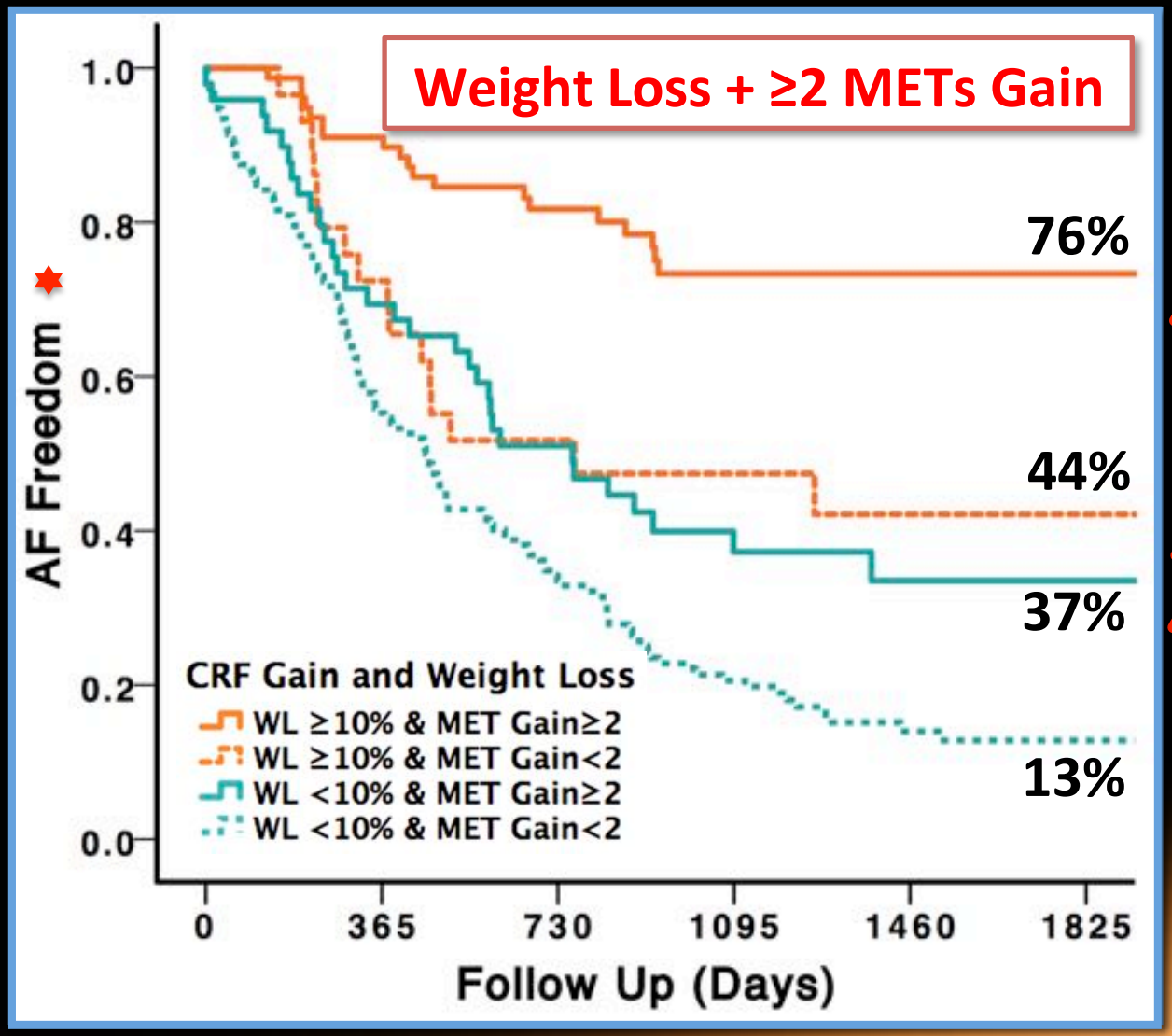
AF Freedom: Drug & Ablation-Free

★ Without AAD or ablation



Days	0	365	730	1095	1460	1825
≥2 MET Gain	127	105	78	52	38	19
<2 MET Gain	181	104	63	36	20	16

Weight Loss and CRF
Drug & Ablation-Free AF freedom

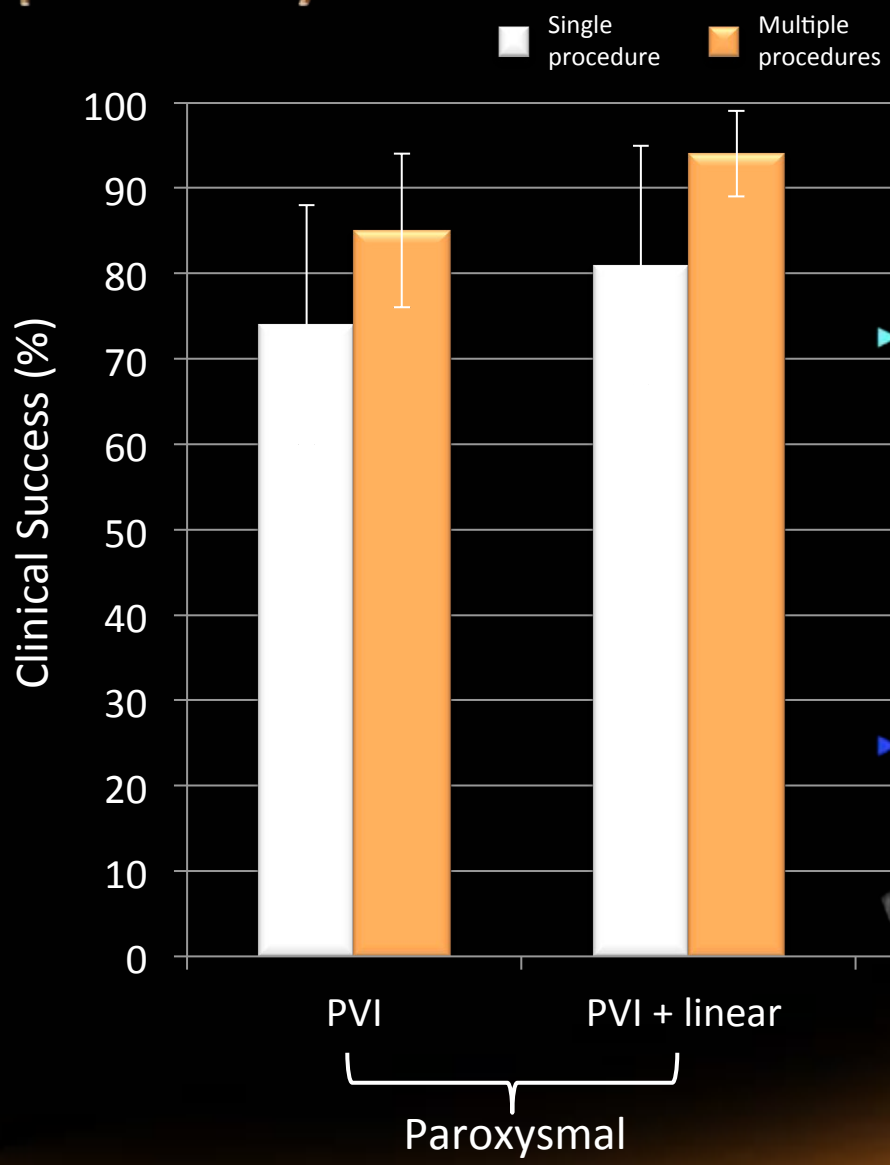


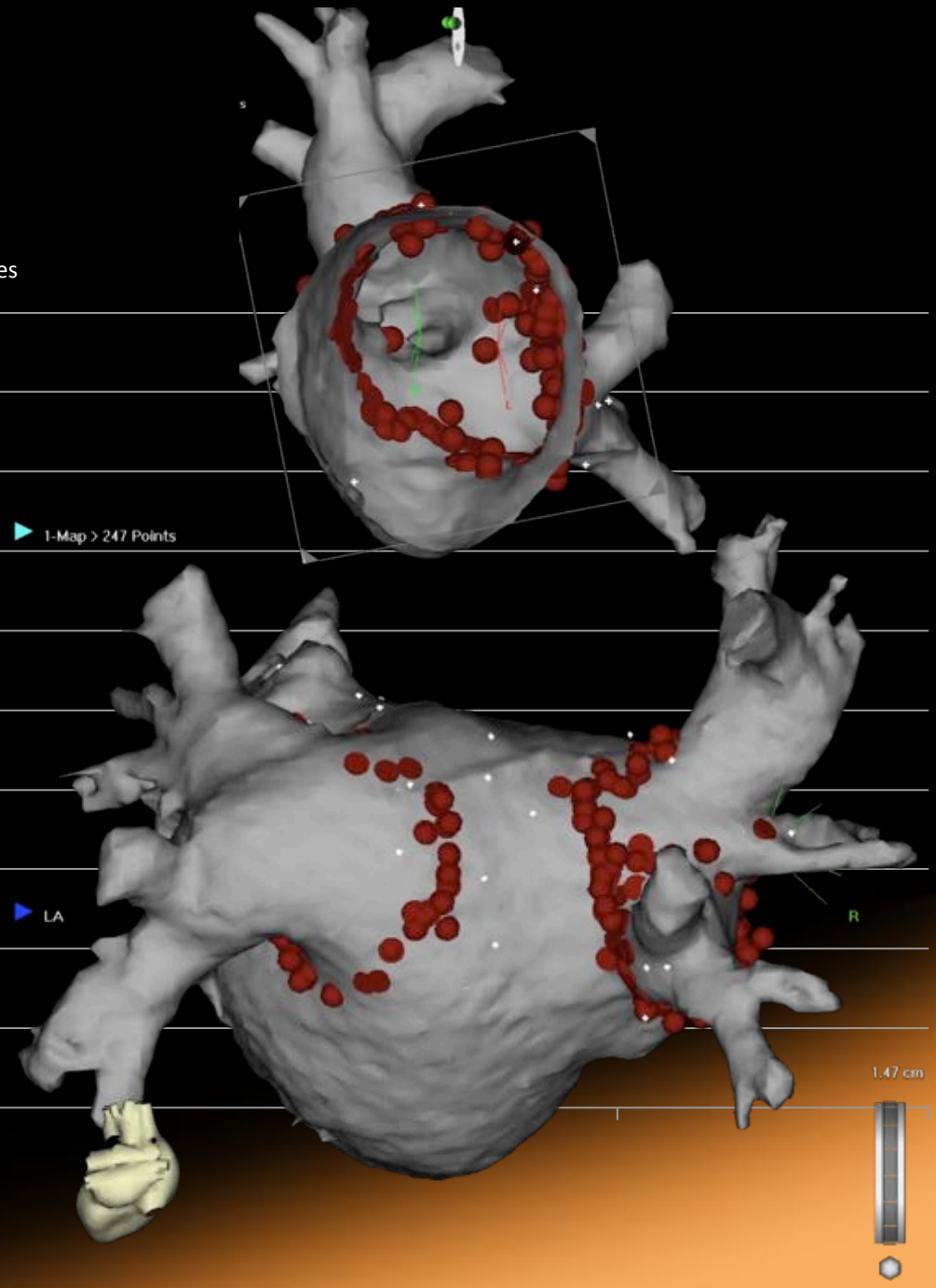
Without AAD or ablation

≥ 2MET
32%

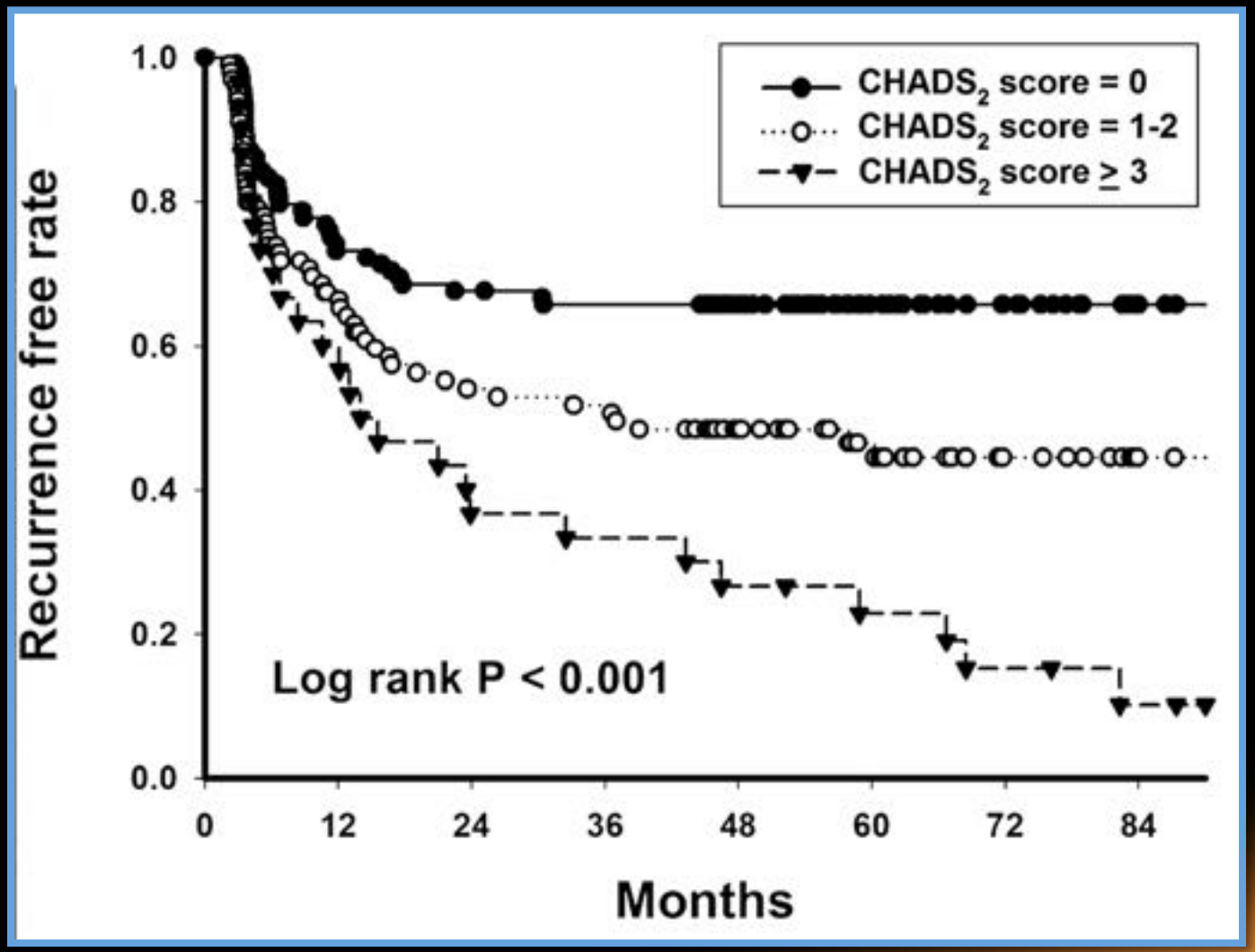
≥1 2MET
24%

Clinical success in paroxysmal AF





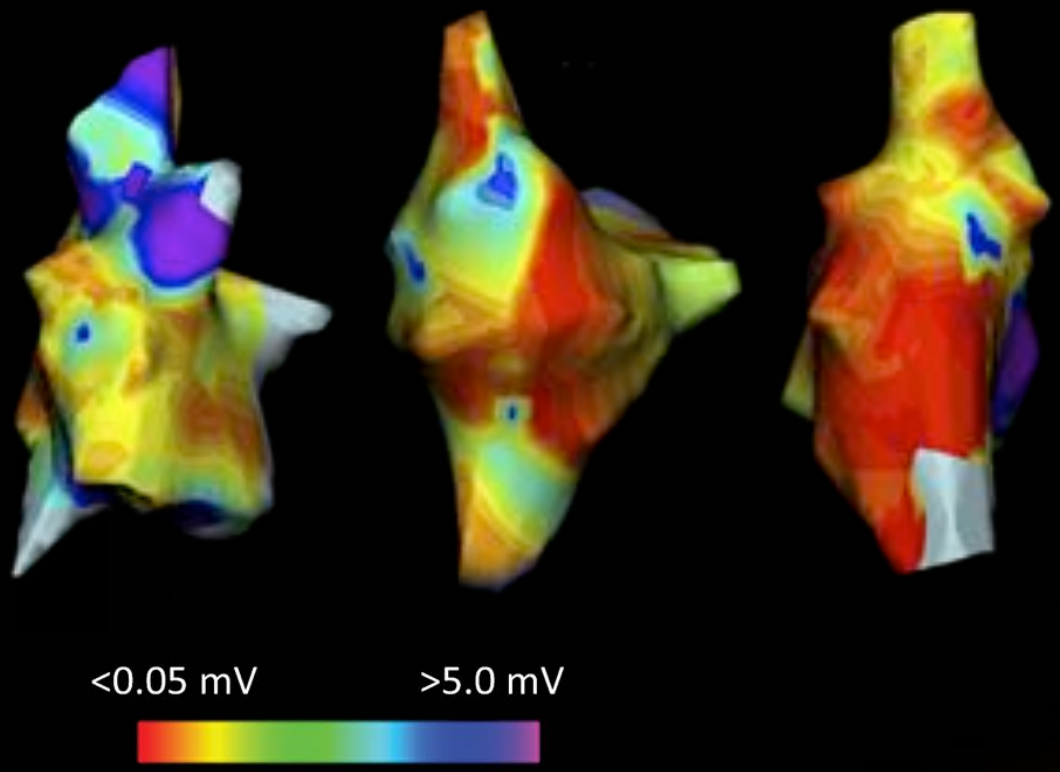
Risk factors & recurrence after ablation

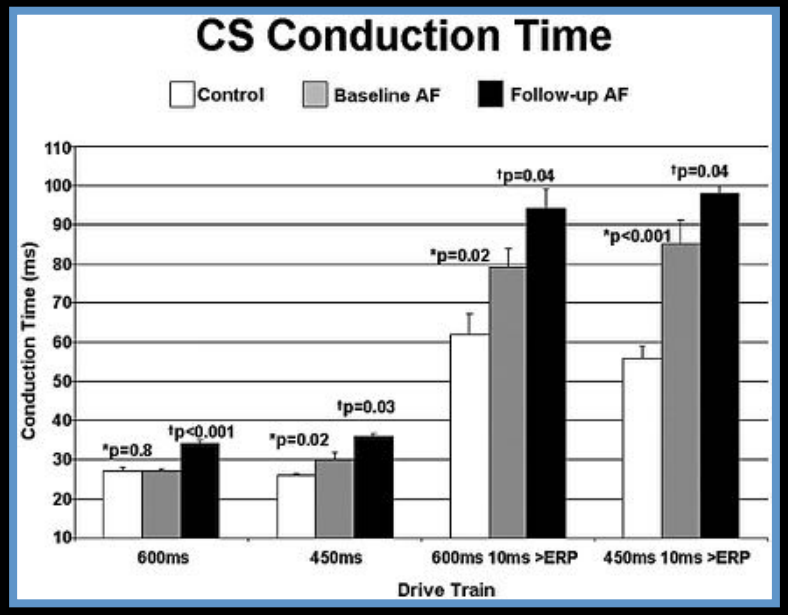


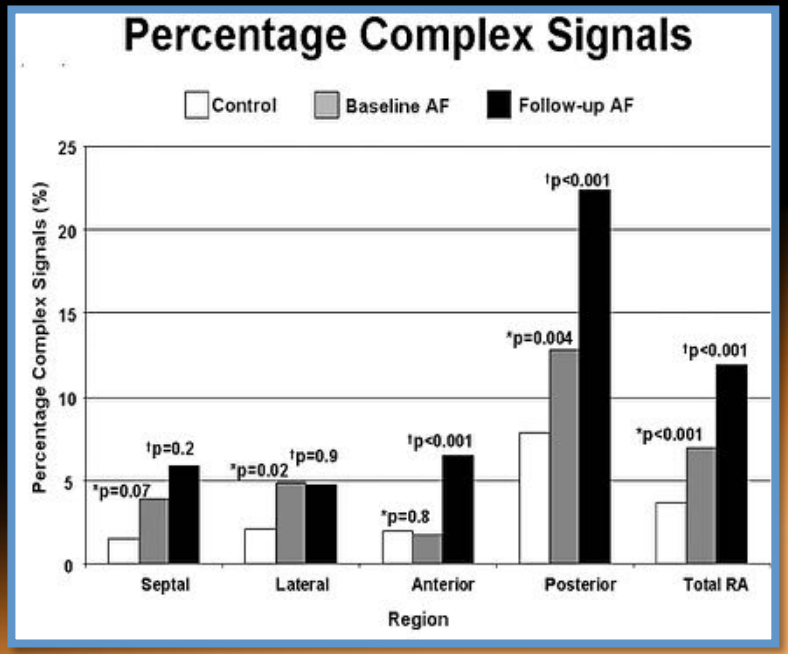
Chao et.al Heart Rhythm 2012

Progressive atrial substrate despite successful ablation

Control Ablation Follow Up







Teh et al, Heart Rhythm 2012

Aggressive Risk Factor Reduction Study for Atrial Fibrillation and Implications for the Outcome of Ablation

The ARREST-AF Cohort Study

Rajeev K. Pathak, MBBS,* Melissa E. Middeldorp,* Dennis H. Lau, MBBS, PhD,* Abhinav B. Mehta, MAcrSr,† Rajiv Mahajan, MD,* Darragh Twomey, MBBS,* Muayad Alasady, MBBS,*† Lorraine Hanley, BSc,* Nicholas A. Antic, MBBS, PhD,‡ R. Doug McEvoy, MBBS, MD,‡ Jonathan M. Kalman, MBBS, PhD,§ Walter P. Abhayaratna, MBBS, PhD,‖ Prashanthan Sanders, MBBS, PhD*

JACC 2014

Late recurrence of AF after AF ablation is due to progression of the underlying substrate

Therefore, aggressive risk factor intervention would improve ablation outcomes

Risk factor management

Weight Management and Exercise

- Structured Program
- Dedicated Clinic
- Meal Plan
- >10% WL
- VLCD if <3% WL at 3 months
- Lifestyle journal
- 30 minutes 3-4 times weekly to 200 Min

Hyperlipidemia

- Life style measures
- At 3 months LDL > 100 mg/dl - start statin
- Add Fibrate if TG > 200 mg/dl
- Start Fibrate if TG > 500 mg/dl

Glucose Tolerance

- Glucose tolerance test
- Lifestyle measures
- HbA1c> 6.5 at 3 months – start Metformin
- Referred to a diabetes clinic

Hypertension

- Measure BP 2-3 times daily, No added salt diet
- Aim of <130/80mmHg at rest and < 200/100 at peak exercise

Sleep Apnea

- Formal overnight sleep study
- AHI≥30/hour – CPAP
- Use Log in diary

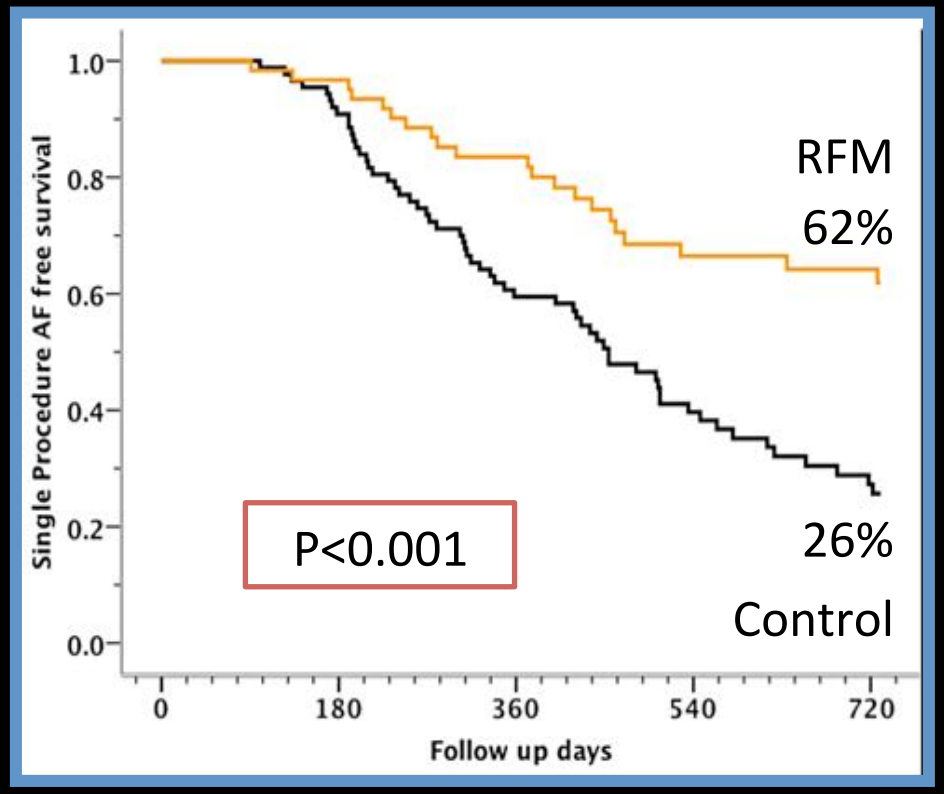
Tobacco and alcohol use

- Smoking cessation
- Alcohol abstinence or reduction to ≤30g/week

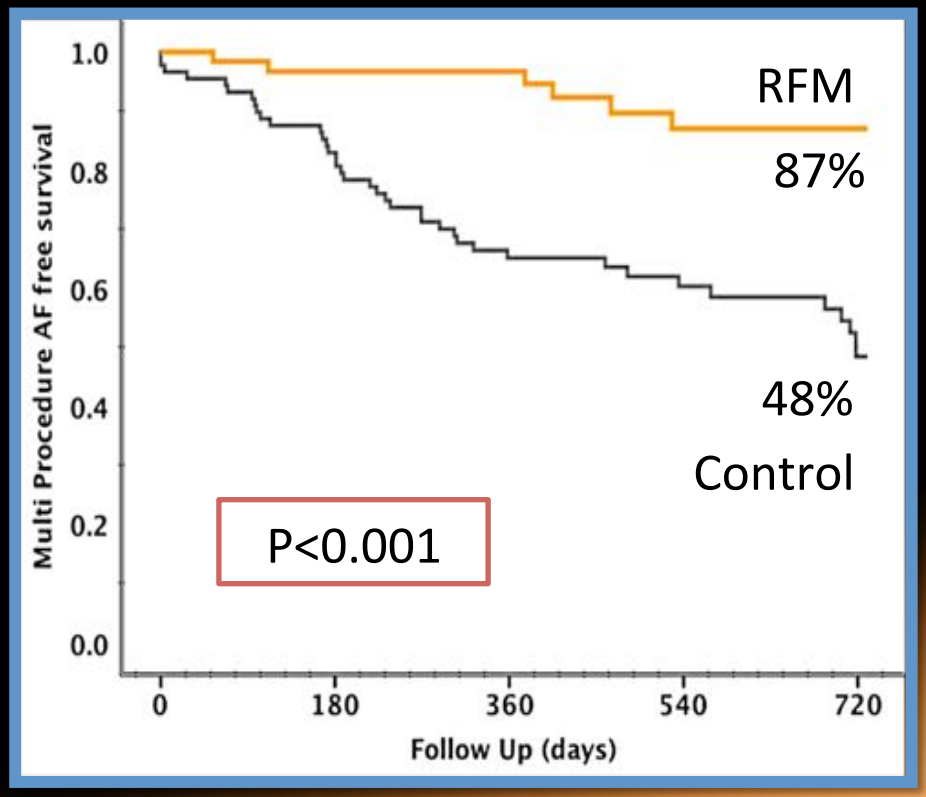
Pathak RK et al. CJC 2015

Aggressive Risk Factor REduction STudy-Implication for AF (ARREST-AF): Implications for Ablation Outcomes

Single procedure success



Multiple procedure success



Risk factors and AF

- AF is a consequence of several, largely modifiable risk factors
- Risk factors are an important determinant of AF development, progression, consequences and response to therapy
- Weight and risk factor management are essential components of AF management (particularly for rhythm control)