Atrial Fibrillation - Sleep Apnea Syndrome

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TEL AVIV, November 1, 2022

1. OSA and atrial fibrillation "cause or consequence?"
    a. Prevalence and incidence arguments
    b. Physiopathological arguments
2. How to treat?
    a. Cardiologist's point of view
    b. OSA
3. Sleep without apnea?
4. Extra « Revolution in the AF »

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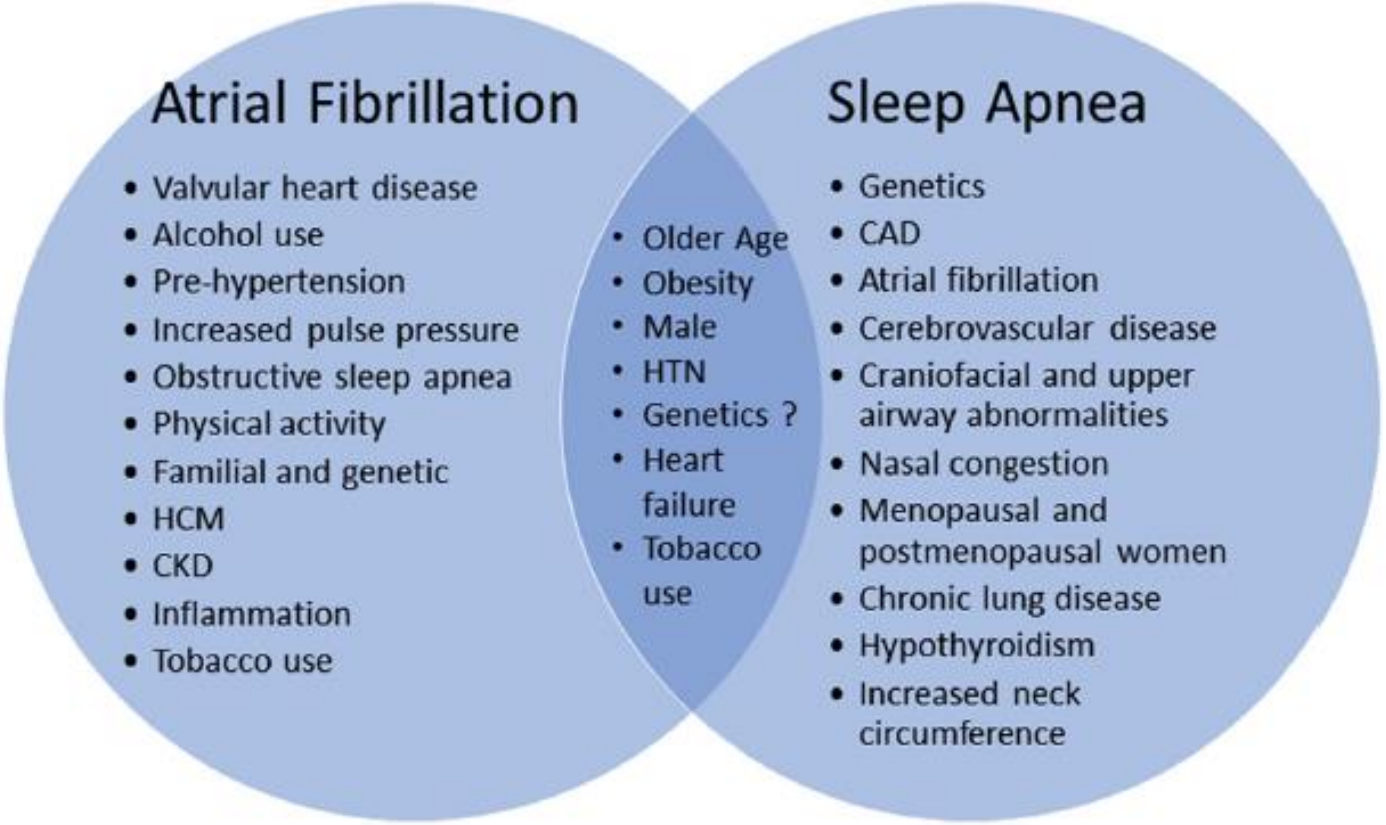
Association AF and OSA= epidemiological chance?

AF 2-3%

OSA 6-38 %



Younghoon Kwon et al. Sleep Medicine Reviews 39 (2018) 134-142

Prevalence and incidence arguments

Table 1
Summary of major studies.

Studies	Study population	Study design	N	SA (%)	Definition of SA	Major findings	Strengths (S) and limitations (L)
Prevalence of SA in AF							
Gami et al. (2004) [2]	Cardiology clinic patients with AF referred for DCCV	Cross-sectional	463 (151 with AF, 312 without AF)	38	Berlin questionnaire	Higher prevalence of OSA in patients with AF vs. matched cardiology clinic patients without AF.	(S) a case-control study with large sample size (L) SA diagnosed by Berlin questionnaire criteria,
Stevenson et al. (2008) [3]	Clinic patients with AF	Cross-sectional	135 (90 with AF, 45 without AF)	54	PSG: AHI ≥ 15 events/h	Higher prevalence of OSA in patients with AF vs. matched electrophysiology clinic patients without AF.	(S) Matched electrophysiology clinic patients without AF as the control group. (L) Small sample size of the control group
Patel et al. (2010) [5]	Multi-center cohort of patients undergoing AF ablation	Retrospective cohort	3000 (all with AF)	21	PSG: AHI > 15 events/h	Presence of OSA increased AF ablation failure rate. Treatment of OSA with CPAP improved the success rate.	(S) Multicenter study with large sample size (L) CPAP therapy was not randomized
Porthan et al. (2004) [7]	Clinic patients with lone AF	Cross-sectional	115 (59 with AF, 56 without AF)	31	PSG: AHI ≥ 15 events/h with symptoms	Prevalence of OSA similar between 'lone AF' vs matched community control subjects.	(S) participants had very low cardiovascular risk and presented as lone AF (L) a small sample size
Longitudinal evaluations of AF in SA							
Gami et al. (2007) [16]	Sleep clinic patients	Retrospective cohort	3542 without AF	74	PSG: AHI > 5 events/h	Magnitude of nocturnal oxygen desaturation associated with an increased risk of future AF.	(S) PSG-defined SA (L) Sleep clinic-based study not applicable to the general population
Lin et al. (2015) [18]	Community-based cohort	Prospective cohort	4395	4	Self-reported PDSA	PDSA associated with an increased risk of future AF.	(S) Multiethnic community-based study (L) SA was not verified by objective PSG

AHI, apnea hypopnea index; AI, apnea index; AF, atrial fibrillation; CPAP, continuous positive airway pressure; DCCV, direct current cardioversion; ECG, electrocardiography; OSA, obstructive sleep apnea; PSG, polysomnography; PDSA, physician-diagnosed sleep apnea; RDI, respiratory disturbance index; SA, sleep apnea.

Younghoon Kwon et al. Sleep Medicine Reviews 39 (2018) 134-142

AF and OSA Association

Prospective study:

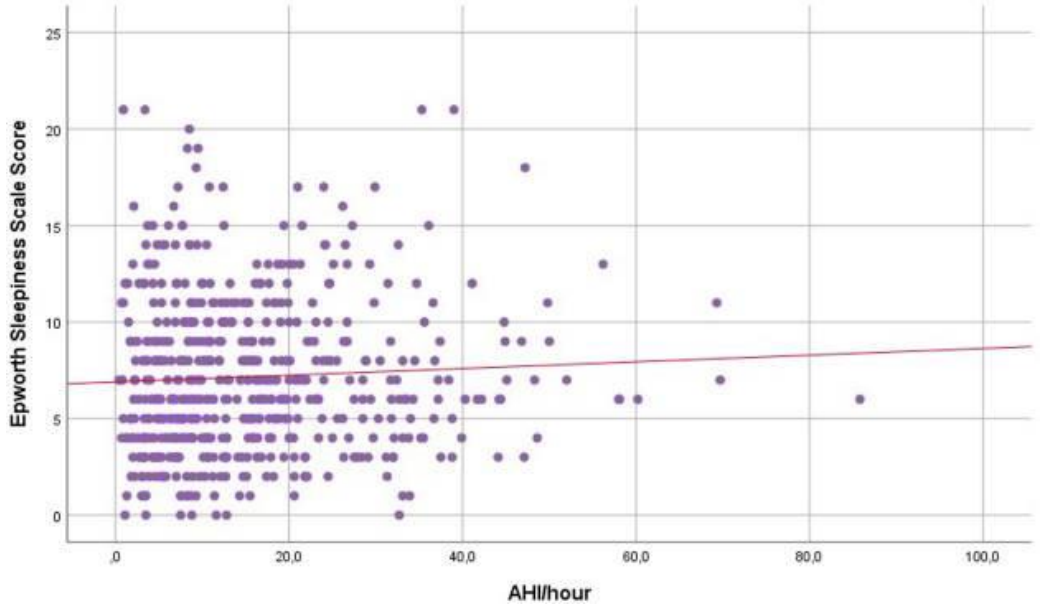
579 pts in paroxysmal AF: screening by polygraphy + clinical scores (Epworth and Berlin)

Results:

1/ 82.7% of AF patients with AHI > 5 and 42.1% with AHI > 15

2/ AF burden and severity of AF symptoms greater if AHI greater than 30

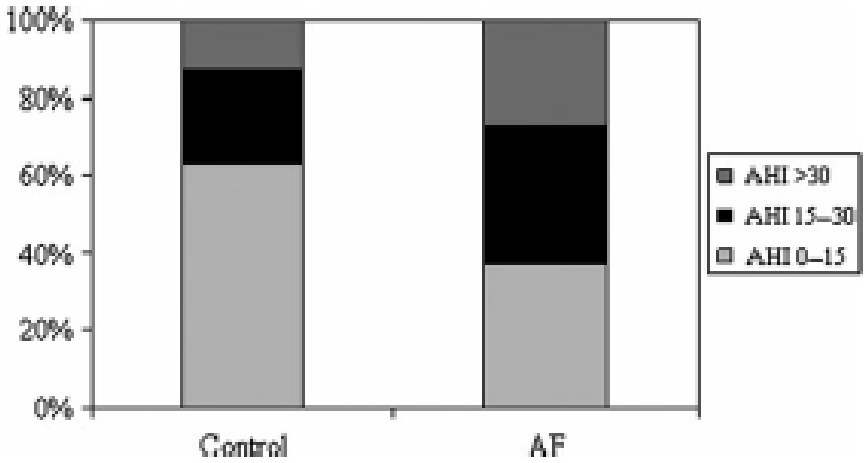
3/ The sleepiness score does not predict AHI

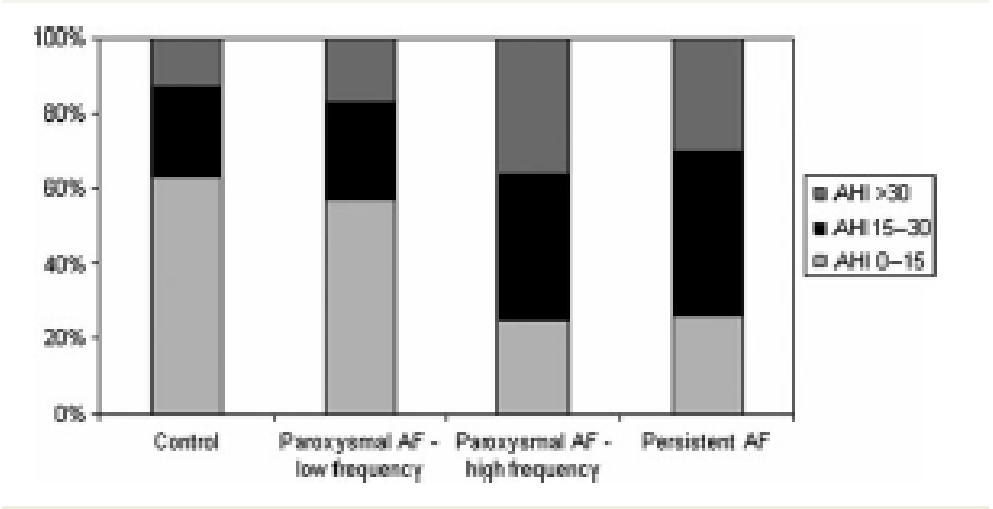


Traaen G.M et al.. Cardiol. Heart Vasc. 2019;26:100447

	AF patients ($n = 90$)	Control patients ($n = 45$)	P-value
Male gender, *n* (%)	74 (82)	37 (82)	
Age, years			
Mean ± SD	56 ± 12	54 ± 11	
Median (IQR)	58 (48–63)	56 (48–62)	
BMI, kg/m^2			
Mean ± SD	27.9 ± 4.5	26.6 ± 3.0	0.08
Median (IQR)	27 (25–30)	26 (24–29)	
Neck circumference, cm			
Mean ± SD	42.5 ± 3.8	41.3 ± 3.8	0.05
Median IQR	42 (40–45)	41 (39.5–44)	
Hypertension, *n* (%)	33 (37%)	12 (27%)	0.14
LV posterior wall thickness, cm			
Mean ± SD	0.95 ± 0.15	0.97 ± 0.14	0.41
Left atrial size, cm			
Mean ± SD	4.14 ± 0.55	3.86 ± 0.50	0.01
AF rhythm			
Paroxysmal, *n* (%)	63 (70)	NA	
Nocturnal, *n* (% of paroxysmal)	17 (27)	NA	
Persistent, *n* (%)	27 (30)	NA	

Prospective cohort of AF patients compared to a control group without AF to evaluate OSA prevalence





Stevenson I et al Eur heart J 2008;29:1662-9

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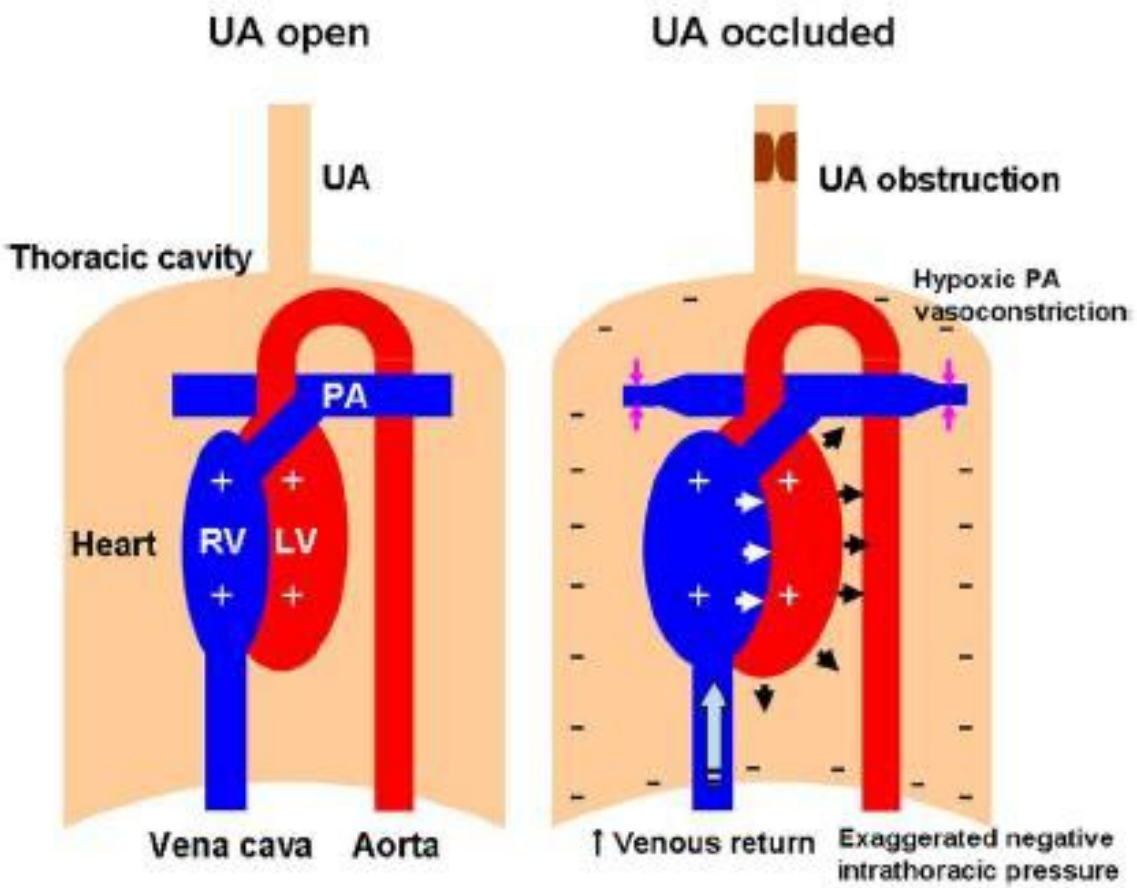
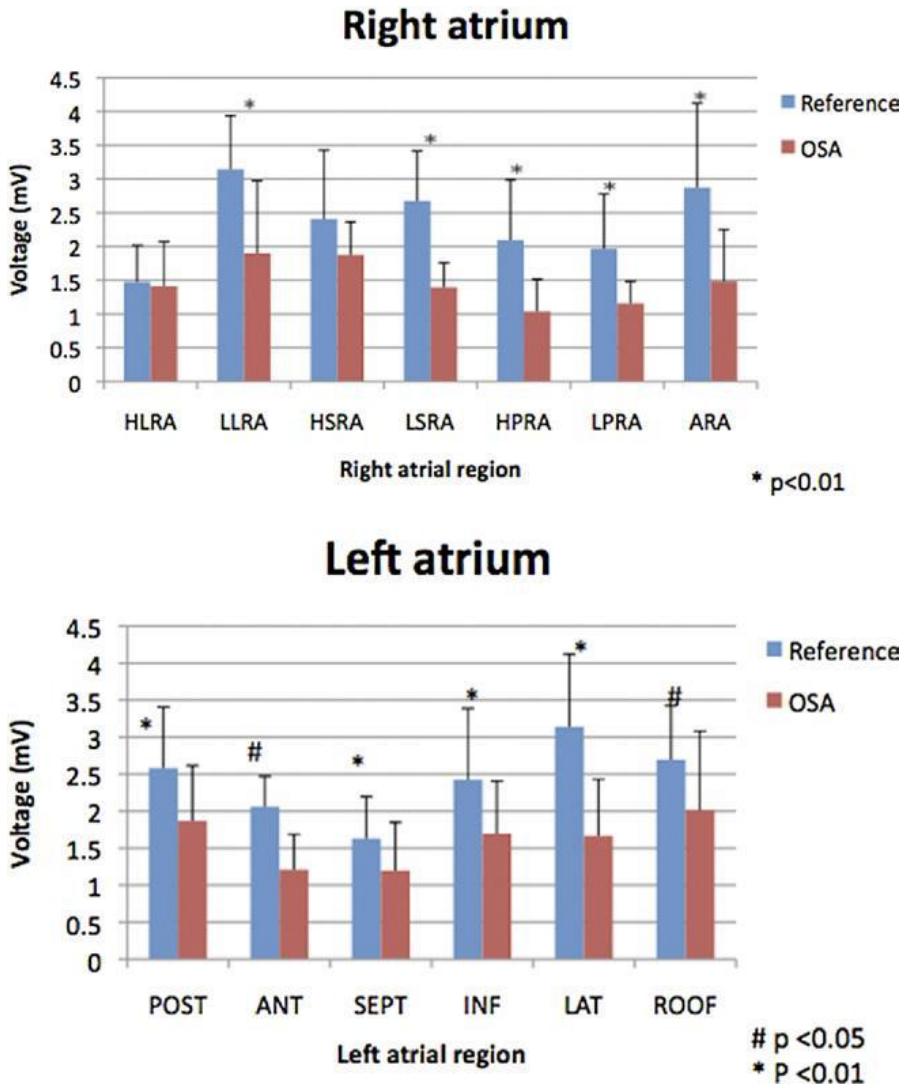
Physiopathological arguments



Kasai T et al J Am Coll Cardiol 2011;57:119-27



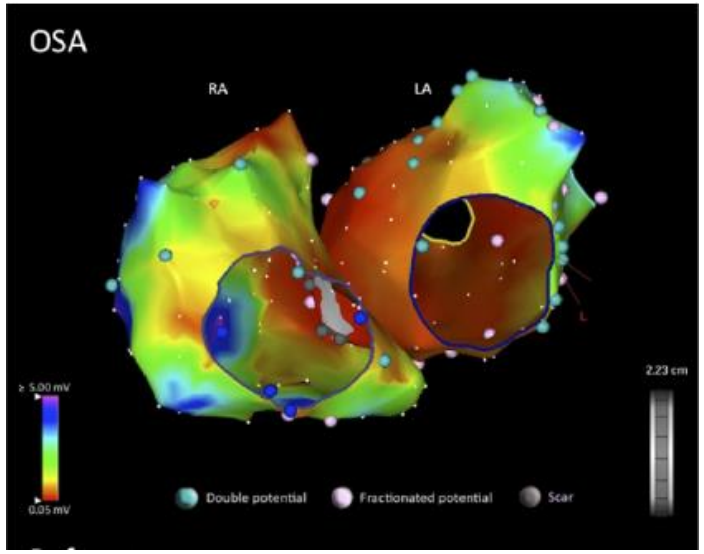
Hany D et al Heart Rhythm 2012;9:321-27

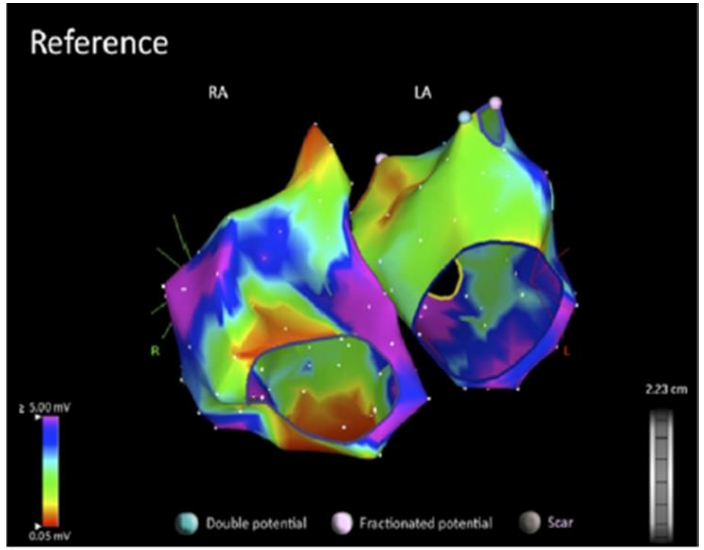
Left atrium in AF patients with OSA: electroanatomical study

SAOS Group:

- More dilated OG (bi-atrial dilation)

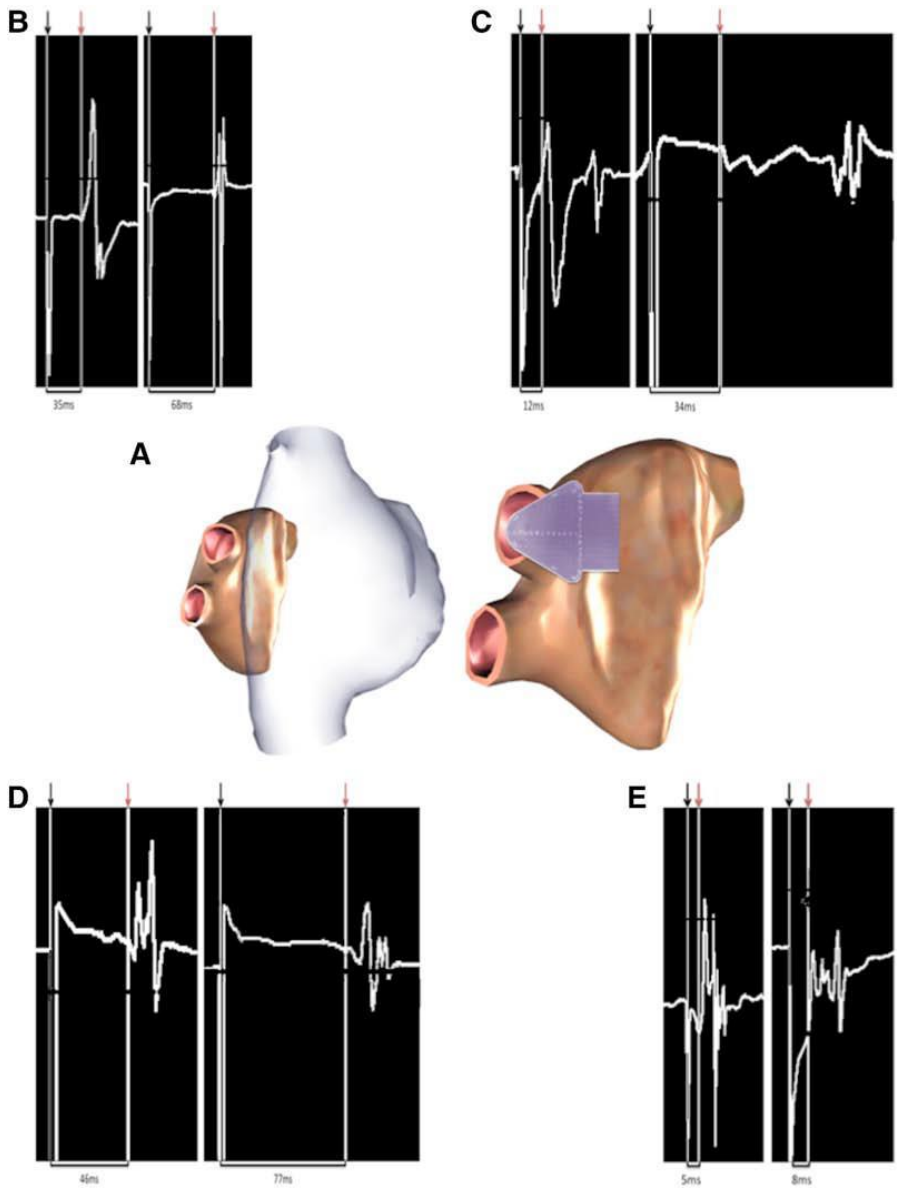
- No more low voltage area corresponding to fibrosis

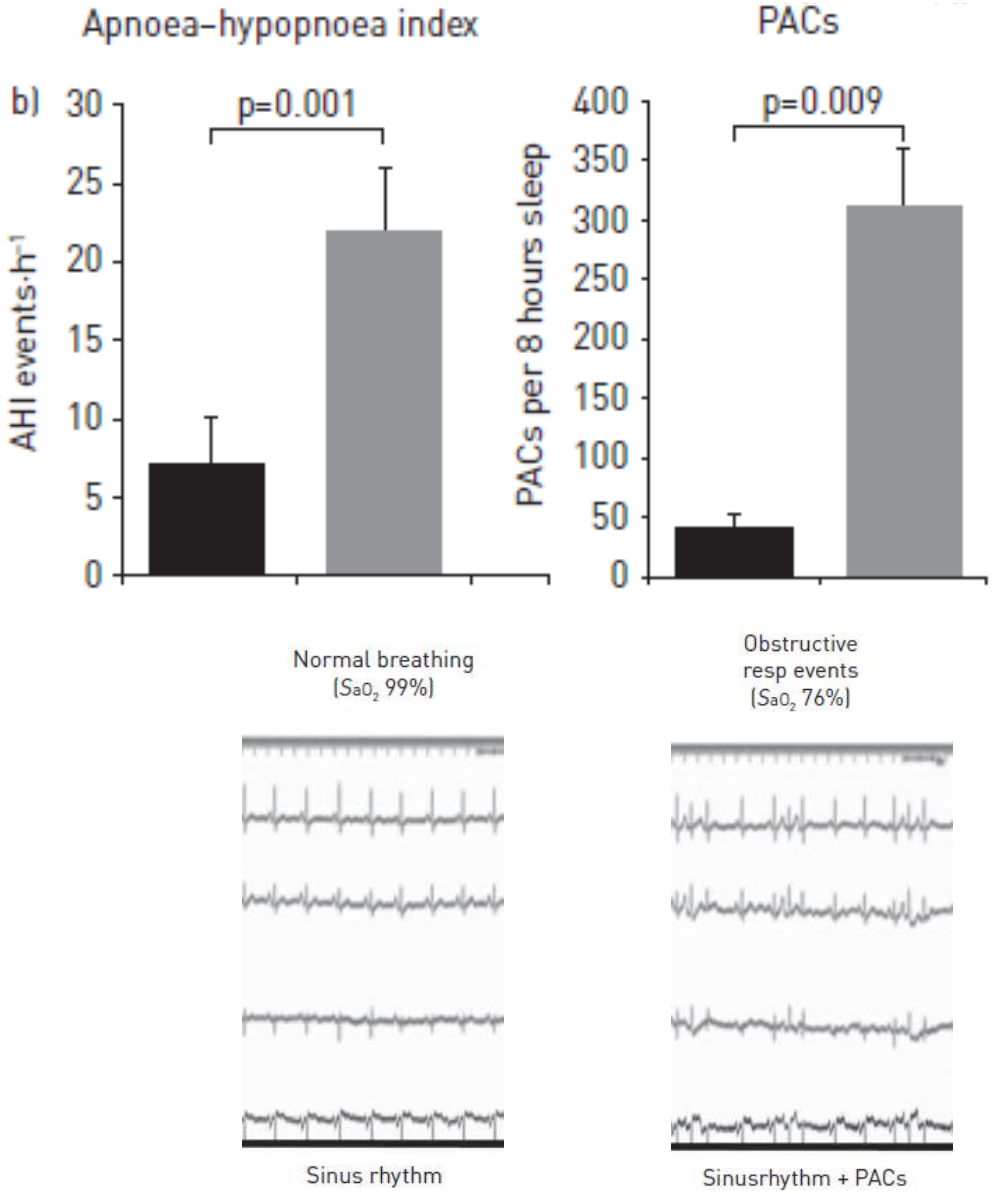




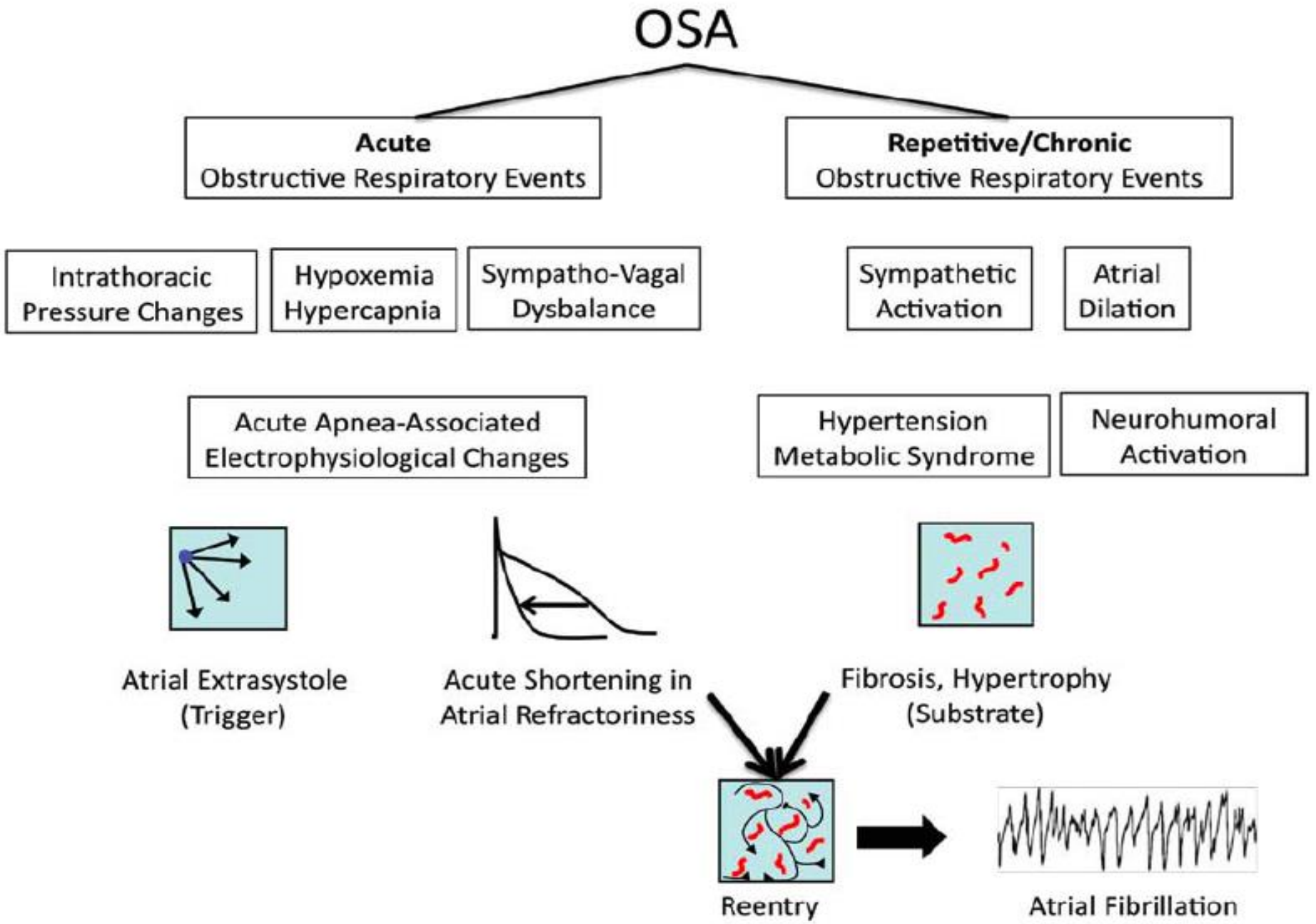
Dimitri H, Heart Rhythm. 2012 Mar;9(3):321-7.

Physiopathological arguments



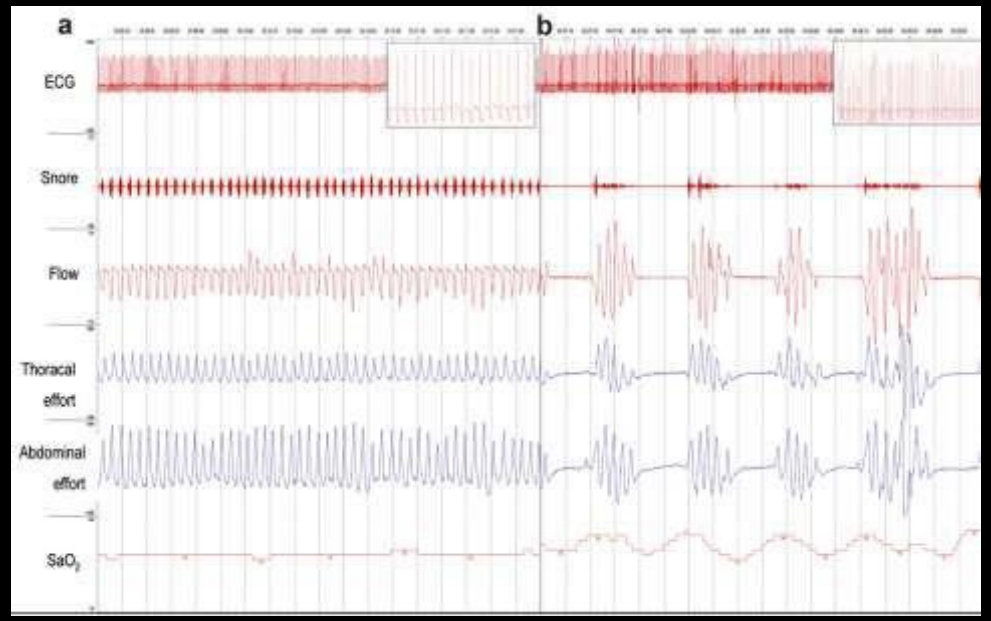


Walters T et al Circ Arrhythm Electrophysiol 2014;7:1189-97 Linz D et al Eur Respir J 2015;45:1332-40


OSA
Acute
Obstructive Respiratory Events
Repetitive/Chronic
Obstructive Respiratory Events
Intrathoracic
Pressure Changes
Hypoxemia
Hypercapnia
Sympatho-Vagal
Dysbalance
Sympathetic
Activation
Atrial
Dilation
Acute Apnea-Associated
Electrophysiological Changes
Hypertension
Metabolic Syndrome
Neurohumoral
Activation
Atrial Extrasystole
(Trigger)
Acute Shortening in
Atrial Refractoriness
Fibrosis, Hypertrophy
(Substrate)
Reentry
Atrial Fibrillation

. Heart failure is the most important contributor to central SAS
30 to 80% of these patients depending on the study (Javaheri *et al*. Semin Repir Crit Care
Med 2005;26:44-55) BUT also AF

. Central SAS can be secondary to AF by secondary hemodynamic instability ++.



Rupprecht S *et al*.
Sleep Med 2008;9:462-4

. Significant association with idiopathic central SAS in one study, superior to OSA: cause or consequence?
Leung RST *et al*. Sleep;28:1543-46

Berlin or Epworth questionnaire and OSA screening for all first detected AF episodes without acute reversible cause particularly in case of ryhythm strategy is mandatory

Classe II a level B

Calkins H et al Heart Rhythm 2017;14:e275-e444

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Table 1
Cohort characteristics stratified by response to antiarrhythmic drugs

Characteristic	Entire Cohort (n = 61)	Nonresponders (n = 31)	Responders (n = 30)
Age (years)	64 ± 9	65 ± 8	64 ± 10
Women	34%	35%	33%
Caucasian	89%	77%	100%
Body mass index (kg/m^2)	34 ± 7	34 ± 8	34 ± 7
Hypertension	66%	65%	67%
Coronary artery disease	31%	25%	38%
Heart failure	20%	22%	17%
AF			
Paroxysmal*	61%	50%	72%
Persistent*	26%	39%	14%
Permanent	12%	11%	14%
Baseline AF burden score	19 ± 8	20 ± 9	18 ± 8
Echocardiographic parameters			
Left atrial dimension (mm)	46 ± 8	47 ± 7	45 ± 9
Left ventricular ejection fraction (%)	50 ± 11	49 ± 12	52 ± 11
Left ventricular hypertrophy	47%	48%	45%
Right ventricular systolic pressure (mm Hg)	38 ± 12	38 ± 12	38 ± 11
Polysomnographic parameters			
AHI (events/hour)*	28 ± 22	34 ± 25	22 ± 18
Minimum oxygen saturation (%)	81 ± 8	80 ± 8	82 ± 9
Portion of total sleep time in rapid eye movement (%)	13 ± 8	15 ± 9	12 ± 7
Severe OSA*	38%	52%	23%

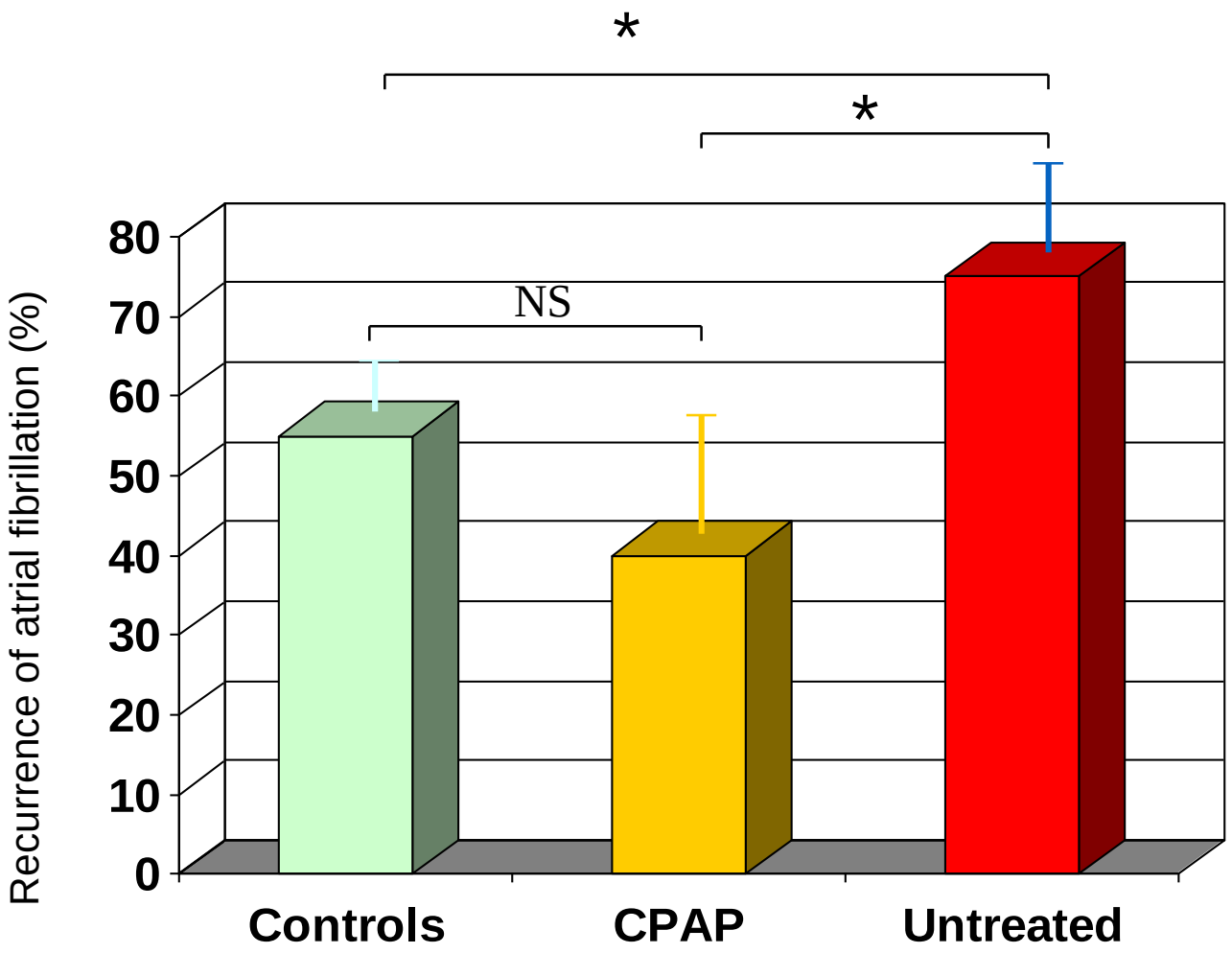
Data are expressed as mean ± SD or as percentages.
* p ≤0.05 for comparison between nonresponders and responders.

Table 2
Cohort characteristics and response to antiarrhythmic drugs stratified by obstructive sleep apnea status

Characteristic	Entire Cohort (n = 61)	Nonsevere OSA (n = 38)	Severe OSA (n = 23)
Age (years)	64 ± 9	64 ± 11	65 ± 7
Women*	34%	42%	22%
Caucasian	89%	90%	87%
Body mass index (kg/m^2)	34 ± 7	33 ± 8	36 ± 6
Hypertension*	66%	58%	78%
Coronary artery disease†	31%	18%	52%
Heart failure	20%	15%	26%
AF			
Paroxysmal	61%	63%	57%
Persistent	25%	21%	30%
Permanent	15%	16%	13%
Baseline AF burden score	19 ± 8	18 ± 9	20 ± 8
Response to AADs‡	49%	61%	30%
Echocardiographic parameters			
Left atrial dimension (mm)	46 ± 8	46 ± 8	47 ± 8
Left ventricular ejection fraction (%)	50 ± 11	52 ± 10	47 ± 14
Left ventricular hypertrophy	47%	43%	52%
Right ventricular systolic pressure (mm Hg)	38 ± 12	38 ± 12	38 ± 12

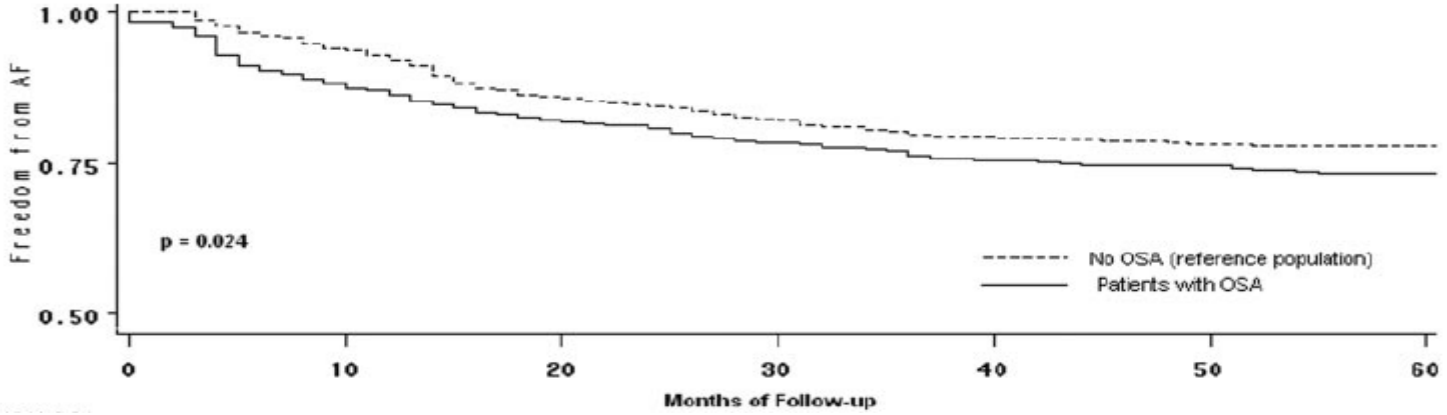
Monahan K et al Am J Cardiol 2012;110:369-72

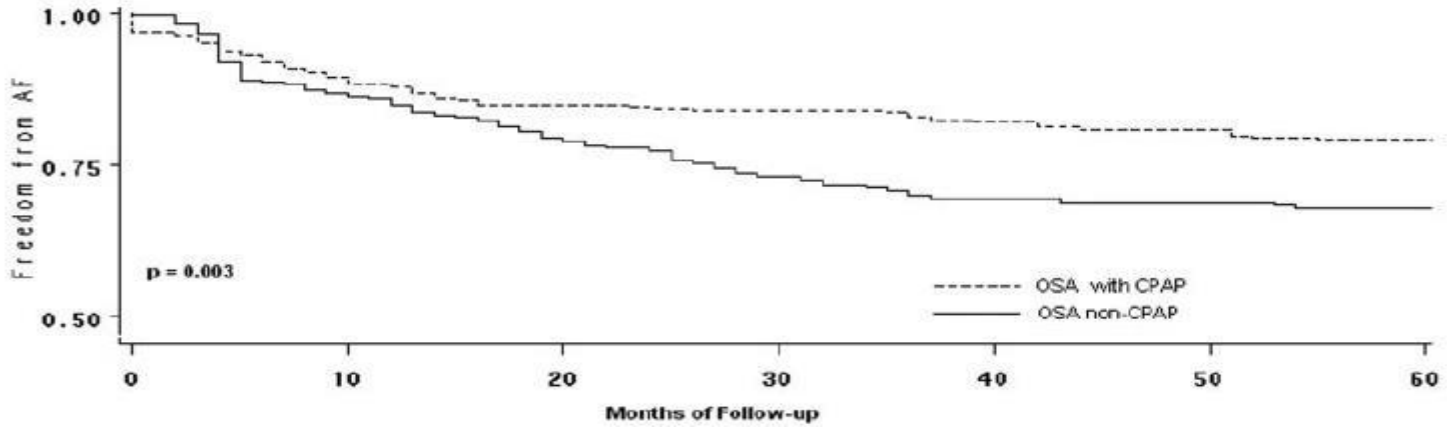
AF recurrence after electrical cardioversion



Kanagala et al, Circulation 2003

AF recurrence after ablation
OSA reduces AF treatments efficiency

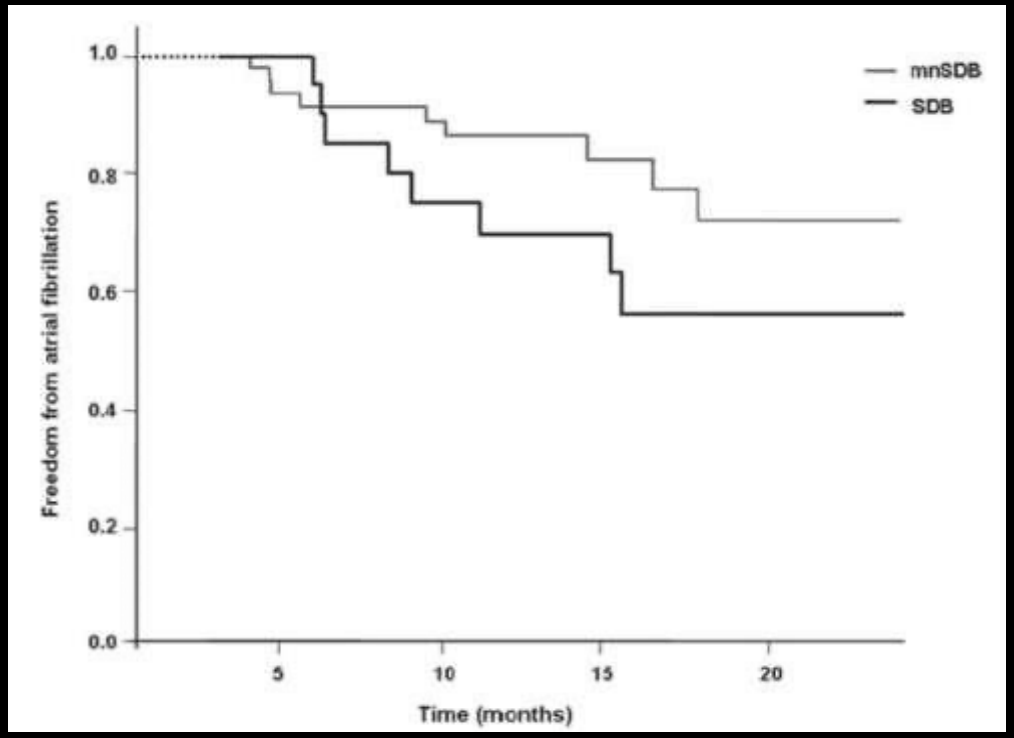




Source	Study Design	AF Ablation Strategy	Follow-up, Mo.
Jongnarangsin et al,[24] 2008	Retrospective, observational	PVI or CFAE	7
Patel et al,[12] 2010	Retrospective, observational	PVI, posterior LA, or SVC	20
Fein et al,[23] 2013	Retrospective, observational	PVI	12
Naruse et al,[26] 2013	Prospective, case-control	PVI, posterior LA, or SVC	18
Neilan et al,[19] 2013	Prospective, case-control	PVI, roof, posterior LA, or CFAE	42

Patel D et al Circ Arrhythm Electrophysiol 2010;3:445-51 Linz D et al JAMA Cardiol 2018;3:532-40

OSA independent factor of recurrence
after an ablation of atrial fibrillation whatever the ablation technique here cryotherapy



Multivariate Analysis of Risk Factors for Recurrence of Atrial Fibrillation in Patients Undergoing Cryoballoon Ablation Therapy

Covariate	Hazard Ratio	95% Conf-L	95% Conf-U	P-Value
Early AF recurrence	8.74	2.76	27.63	<0.001
Persistent atrial fibrillation	7.16	2.22	23.11	<0.001
Class III antiarrhythmic drugs	3.63	1.27	10.33	0.02
Sleep disordered breathing (AHI ≥ 15 per hour)	3.20	1.14	8.95	0.03

Bitter et al. *J Cardiovasc Electrophysiol* 2012;23:18

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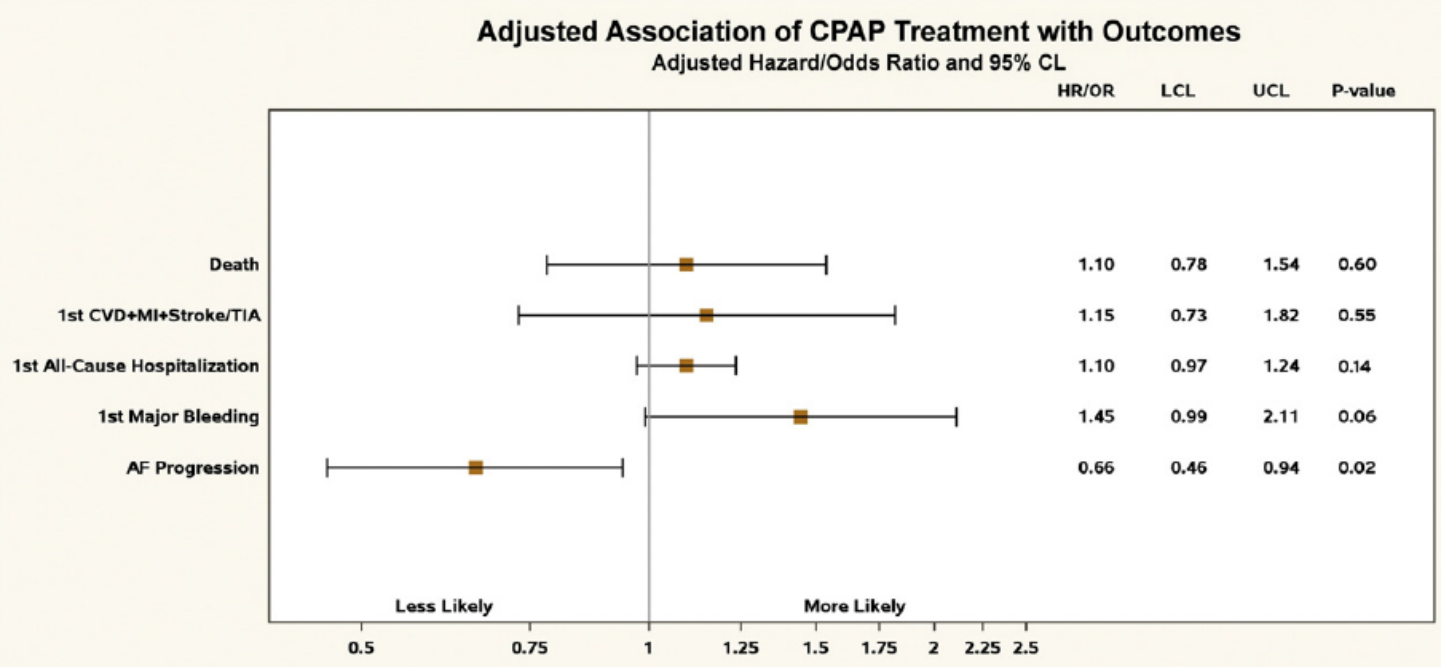
Interest of CPAP in the treatment of AF

ORBIT AF



10 000pts in AF
18% of pts with AF have OSA
58% use of CPAP
>>> beneficial effect of CPAP on AF progression

Holmqvist F et al. Am Heart J. 2015 May

ESC European Society of Cardiology

FA 2020 Guidelines: place of OSA

Recommendations	Class[a]	Level[b]
Opportunistic screening for AF should be considered in patients with OSA.[172]	IIa	C
Optimal management of OSA may be considered, to reduce AF incidence, AF progression, AF recurrences, and symptoms.[650,651,1047–1051]	IIb	C

Does CPAP improve AF treatment ?

Impact of CPAP on the Atrial Fibrillation Substrate in Obstructive Sleep Apnea

The SLEEP-AF Study

FIGURE 1 Consort Diagram

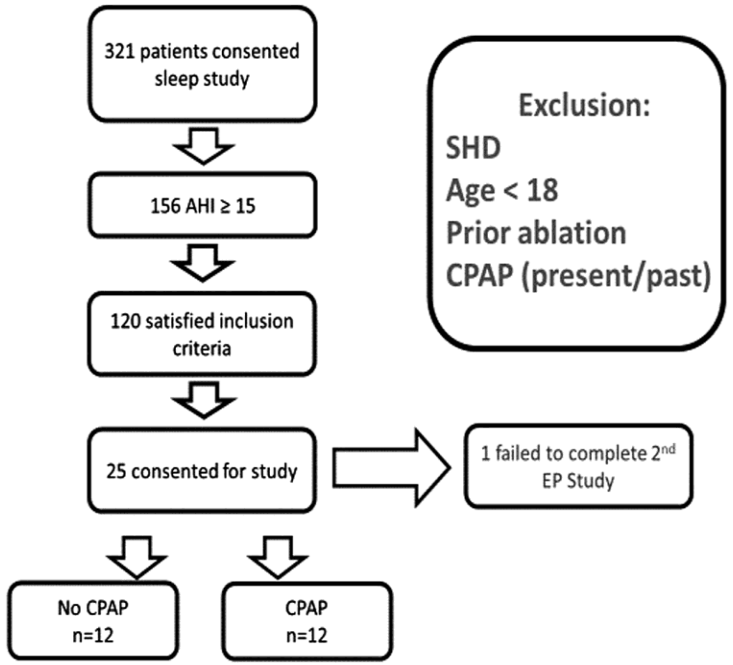


TABLE 1 Baseline Characteristics

	No CPAP (n = 12)	CPAP (n = 12)	*P* Value
Age, y	59 ± 9	59 ± 9	0.99
Male	11 (92)	10 (91)	1.00
Persistent AF	7 (58)	4 (36)	0.41
Hypertension	9 (75)	7 (64)	0.67
Diabetes	3 (25)	1 (9)	0.60
Cholesterol	3 (25)	5 (46)	0.40
Stroke/TIA	1 (9)	1 (9)	1.00
CHA_2DS_2-VASc	1.7 ± 1.3	1.7 ± 1.6	0.95
AHI, events/h	40 ± 20	45 ± 27	0.62
OSA severity			1.00
Moderate	3 (25)	4 (33)	
Severe	9 (75)	8 (66)	

Values are mean ± SD or n (%).

AHI = apnea-hypopnea index; CPAP = continuous positive airway pressure; OSA = obstructive sleep apnea; TIA = transient ischemic attack.

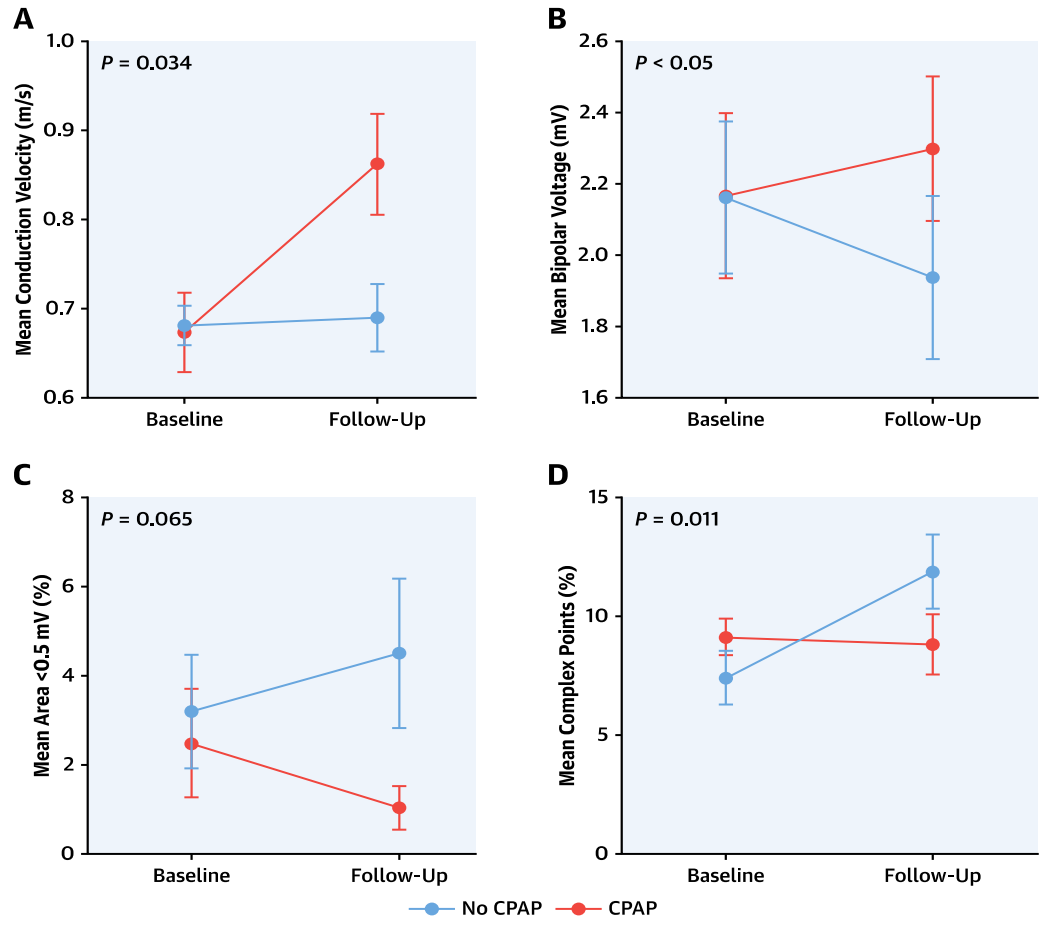
TABLE 2 CPAP Compliance Was High in the Treatment Group

Δ AHI from baseline, events/h	31 ± 23
Device usage, %	79 ± 19
Days device used ≥4 h, %	63 ± 21
Average usage, min/d	268 ± 91

Values are mean ± SD.

Abbreviations as in Table 1.

CENTRAL ILLUSTRATION CPAP Reverses Electrical Remodeling in AF



Nalliah CJ, et al. J Am Coll Cardiol EP. 2022;8(7):869-877.

Continuous positive airway pressure (CPAP) therapy results in significantly **(A)** higher mean conduction velocity, **(B)** higher bipolar voltage, **(C)** lower left atrial surface area <0.5 mV, and **(D)** fewer complex points. *P* values refer to group × time interaction. AF = atrial fibrillation.

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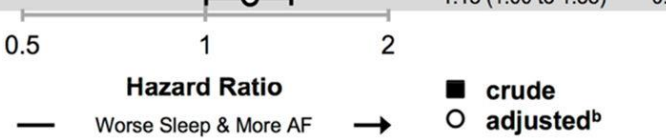
Sleep Characteristics that Predict Atrial Fibrillation

Sleep Characteristic	HR for AF (95% CI)	P Value
Trouble falling asleep	1.11 (0.99 to 1.24)	0.09
	1.02 (0.89 to 1.18)	0.76
Nighttime Awakening	1.33 (1.19 to 1.47)	<0.001
	1.33 (1.17 to 1.51)	<0.001
Early Awakening	1.17 (1.06 to 1.30)	0.003
	1.11 (0.98 to 1.26)	0.11
Groggy or Sleepy in the Daytime	1.14 (1.02 to 1.29)	0.025
	1.01 (0.88 to 1.17)	0.84

Sleep Characteristic[a]	OR for AF (95% CI)	P Value
PSQI total score (↑)	1.16 (1.04 to 1.29)	0.010
	0.92 (0.75 to 1.13)	0.44
Sleep onset latency (↑)	1.18 (1.06 to 1.31)	0.002
	1.17 (1.03 to 1.32)	0.013
Sleep efficiency (↓)	1.13 (1.02 to 1.26)	0.023
	1.04 (0.91 to 1.20)	0.58
PSQI quality sub-score (↑)	1.15 (1.03 to 1.28)	0.012
	1.06 (0.90 to 1.24)	0.50
Frequent nighttime awakening	1.56 (1.26 to 1.94)	<0.001
	1.47 (1.14 to 1.89)	0.003
Frequent nighttime bathroom use	1.28 (1.02 to 1.61)	0.031
	1.08 (0.85 to 1.39)	0.52

PSG Sleep Characteristic[a]	HR for AF (95% CI)	p value
Sleep duration (↓)	1.11 (0.95 to 1.29)	0.17
	0.96 (0.79 to 1.17)	0.69
Sleep efficiency (↓)	1.05 (0.89 to 1.24)	0.57
	0.80 (0.63 to 1.01)	0.06
Sleep onset latency (↑)	1.10 (0.95 to 1.27)	0.21
	1.07 (0.87 to 1.32)	0.53
% Stage N1 (↓)	0.95 (0.84 to 1.08)	0.43
	1.03 (0.88 to 1.22)	0.68
% Stage N2 (↓)	0.91 (0.80 to 1.04)	0.17
	1.02 (0.87 to 1.20)	0.78
% Slow-wave-sleep (↓)	1.02 (0.89 to 1.15)	0.81
	0.88 (0.75 to 1.04)	0.13
% REM sleep (↓)	1.20 (1.05 to 1.36)	0.006
	1.18 (1.00 to 1.38)	0.047



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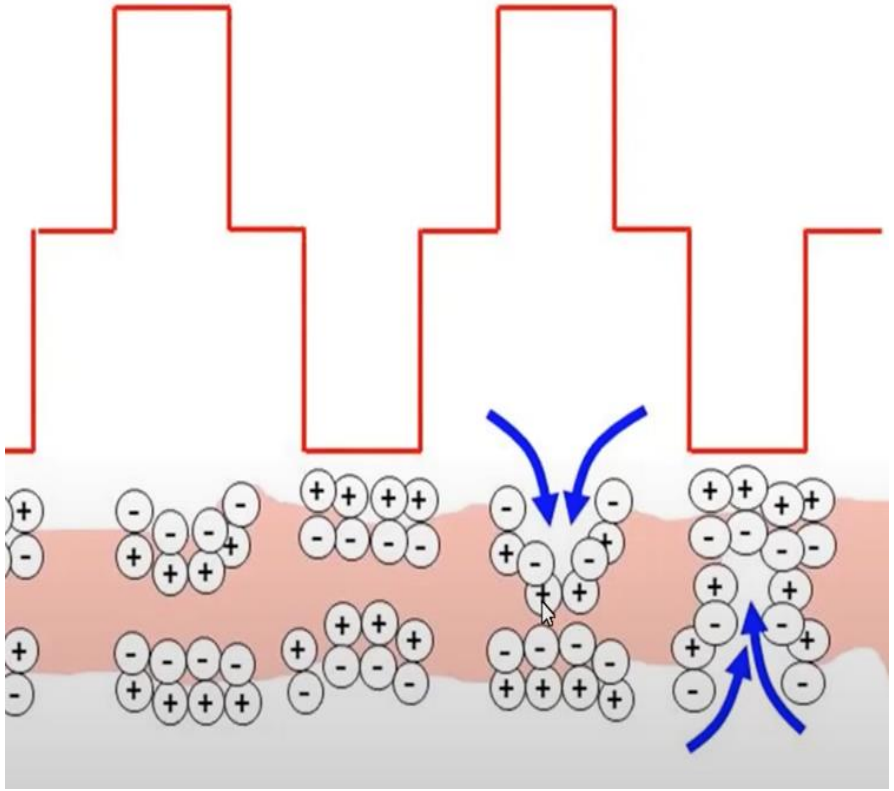
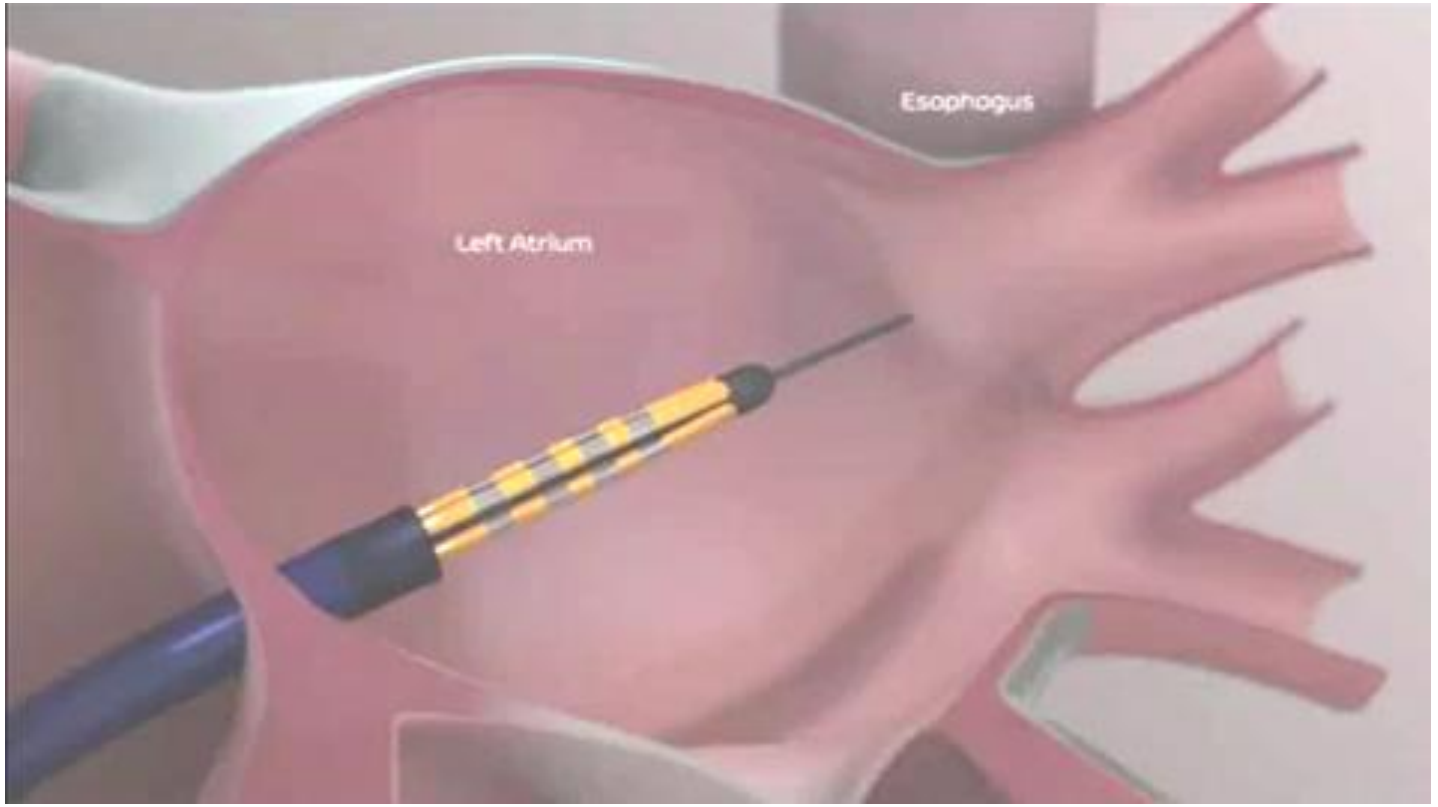
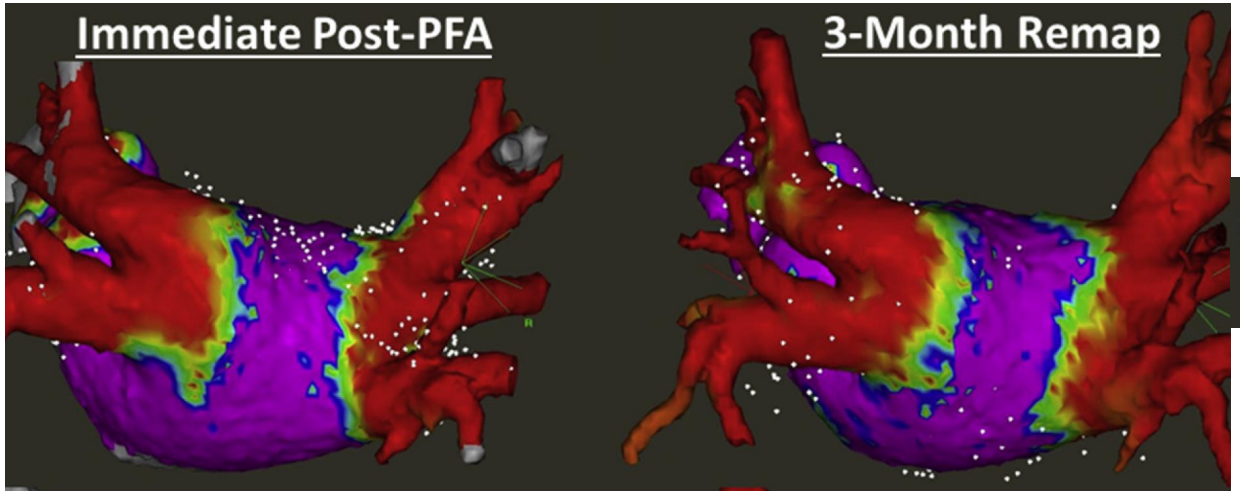
Electroporation (« Pulsed field Ablation »)





Reddy VY et al, J Am Coll Cardiol. 2020 Sep, 76 (9) 1068–1080



Reddy VY et al, J Am Coll Cardiol. 2019;74(3):315-326.

- Systematic detection is recommanded
- Tight corelation between AF and OSA
- OSA reduces all therapeutic intervention efficiency in AP
- CPAP seems to be usefull
- Enlist the patient in a general AF treatment program (weight loss, OSA, compliance)

MERCI DE VOTRE ATTENTION