CardioVascular Institute

Beth Israel Deaconess Medical Center

A teaching hospital of Harvard Medical School

Sleep Apnea and Non-PV Triggers:

KHRS 2017

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1. [**Atrial fibrillation** and obstructive **sleep apnea**: a fortuitous association?].
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   Rev Med Suisse. 2014 Oct 15;10(446):1913-7. Review. French.
   PMID: 25438374
   Similar articles

2. Obstructive **sleep apnea** and **atrial fibrillation**: understanding the connection.
   Oza N, Baveja S, Khayat R, Houmsse M.
   Expert Rev Cardiovasc Ther. 2014 May;12(5):613-21. doi: 10.1586/14779072.2014.902748. Epub 2014 Apr 15. Review.
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3. Obesity, Exercise, Obstructive **Sleep Apnea**, and Modifiable Atherosclerotic Cardiovascular Disease Risk Factors in **Atrial Fibrillation**.
   Miller JD, Aronis KN, Chrispin J, Patil KD, Marine JE, Martin SS, Blaha MJ, Blumenthal RS, Calkins H.
   J Am Coll Cardiol. 2015 Dec 29;66(25):2899-906. doi: 10.1016/j.jacc.2015.10.047. Review.
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Nocturnal Desaturation is Associated With **Atrial Fibri** [J Clin Sleep Med. 2017]

See more...

Sleep Apnea and AF:

Is the link real ?

- Cause and effect relationship
- Co- travelers (shared risk factors)

Atrial Fibrillation and Sleep Apnea

1. Association between AF and OSA

2. Mechanistic relationship between AF and OSA

3. Substrate and triggers of AF in patients with OSA

   - Implication for therapy (screening, ablation)

Prevalence of AF in patients with OSA

Sleep Heart Health Study

- Prospective longitudinal cohort in 6,400 participants
- Aimed to assess arrhythmia prevalence in patients with SA
- All patients underwent sleep testing
- 228 individuals with severe SA were compared to 338 individuals without OSA

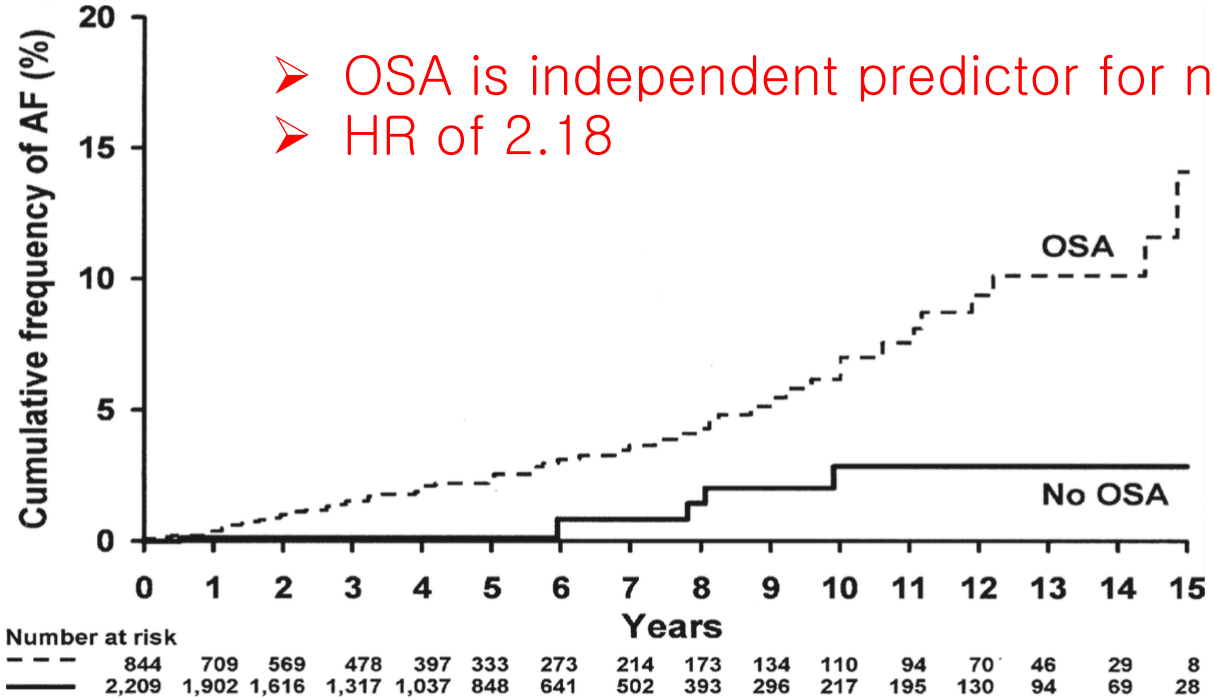
- ➢ Patients with SA had ~5 fold increased risk of AF
- ➢ Adjusted risk (Age, BMI, CAD) of 4.02 [1.03–15.74]; 95%CI)

EJ Benjamin, Am J Respir Crit Care Med 2006

Incidence of AF in patients with OSA

Olmsted County sleep study registry

3500 individuals without AF at baseline followed longitudinally



- OSA is independent predictor for new AF
- HR of 2.18

Gami AS, JACC 2007

The prevalence of OSA in patients with AF

Unknown (10-70%) based on retrospective studies

Prospective evaluation (unpublished data)

- Prospective Multicenter study (Boston, Texas)
- Sleep study in all patients refereed for AF ablation
- 125 consecutive patients with paroxysmal and persistent AF without previous diagnosis of OSA
- Home sleep testing

The prevalence of OSA in patients with AF

Prospective evaluation (unpublished data)

- Prospective Multicenter study (Boston, Texas)
- Sleep study in all patients refereed for AF ablation
- 125 consecutive patients with paroxysmal and persistent AF without previous diagnosis of OSA

- 45% have sleep apnea
- 25% have ≥moderate OSA

Unpublished data

Mechanistic Relationship

1. Negative intra-thoracic pressure

2. Autonomic imbalance

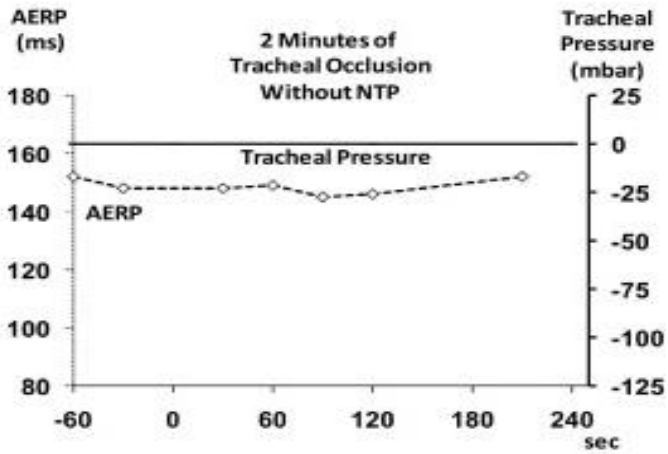
Acute effects

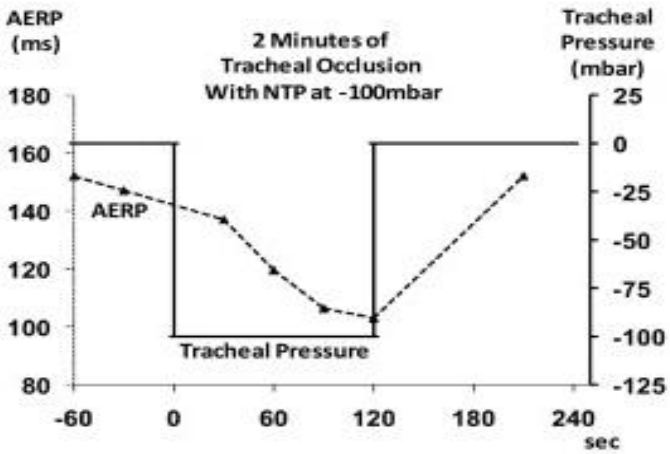
3. Structural remodeling

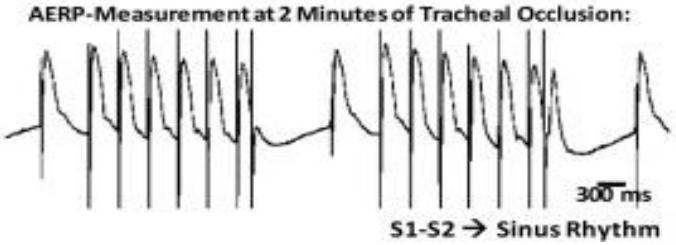
Chronic effects

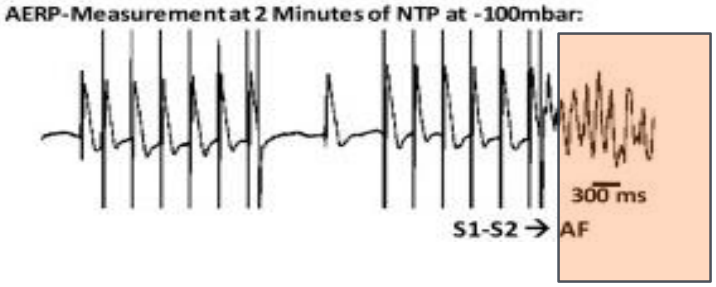
Mechanistic Relationship

Acute effects of OSA are mediated by changes in intrathoracic Pressures





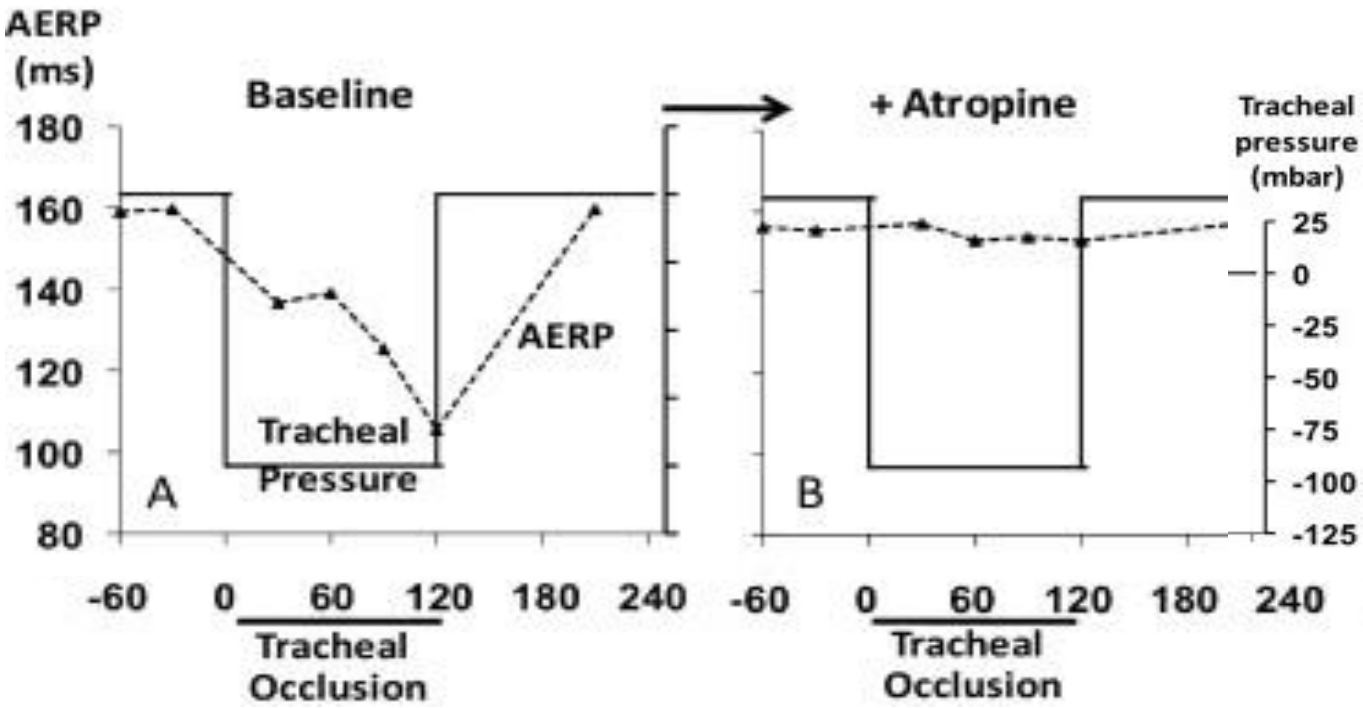




Linz D, Heart Rhythm 2011

Mechanistic Relationship

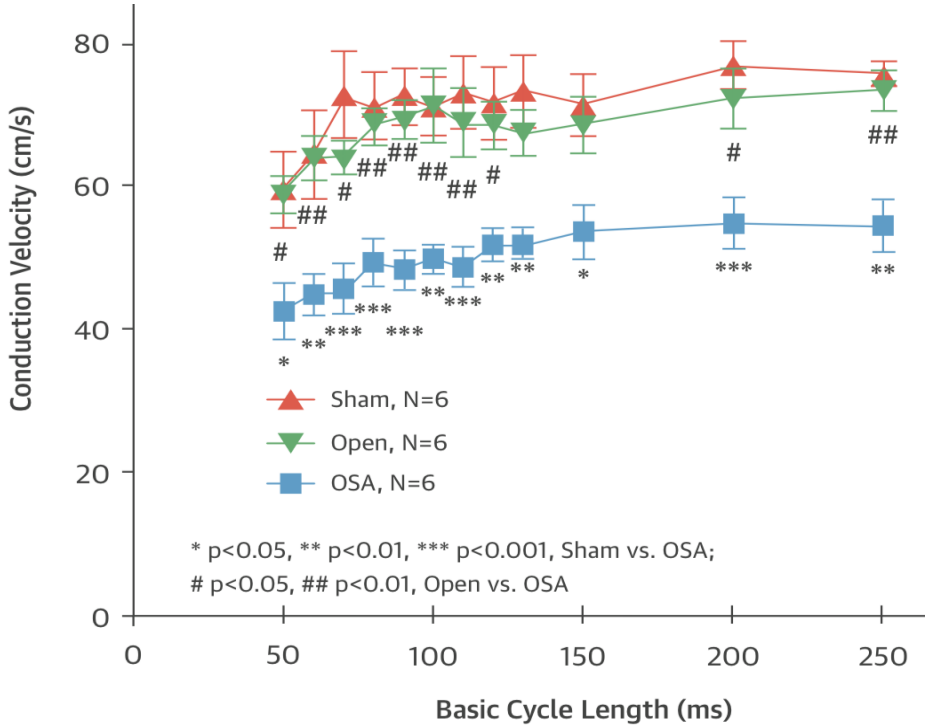
Effect of vagal blockade on AERP and AF inducibility

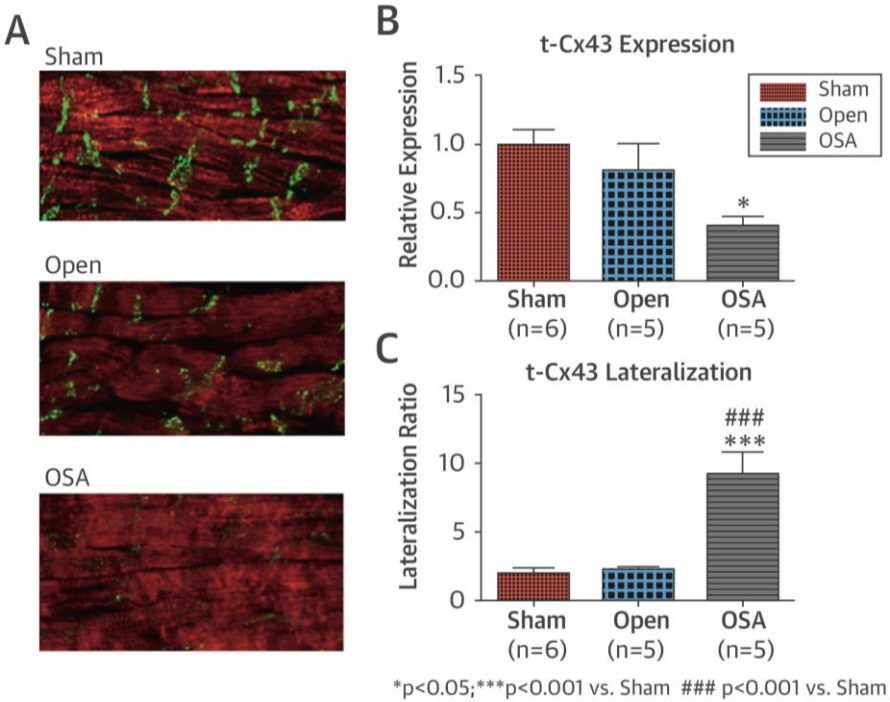


Linz D, Heart Rhythm 2011

Mechanistic Relationship

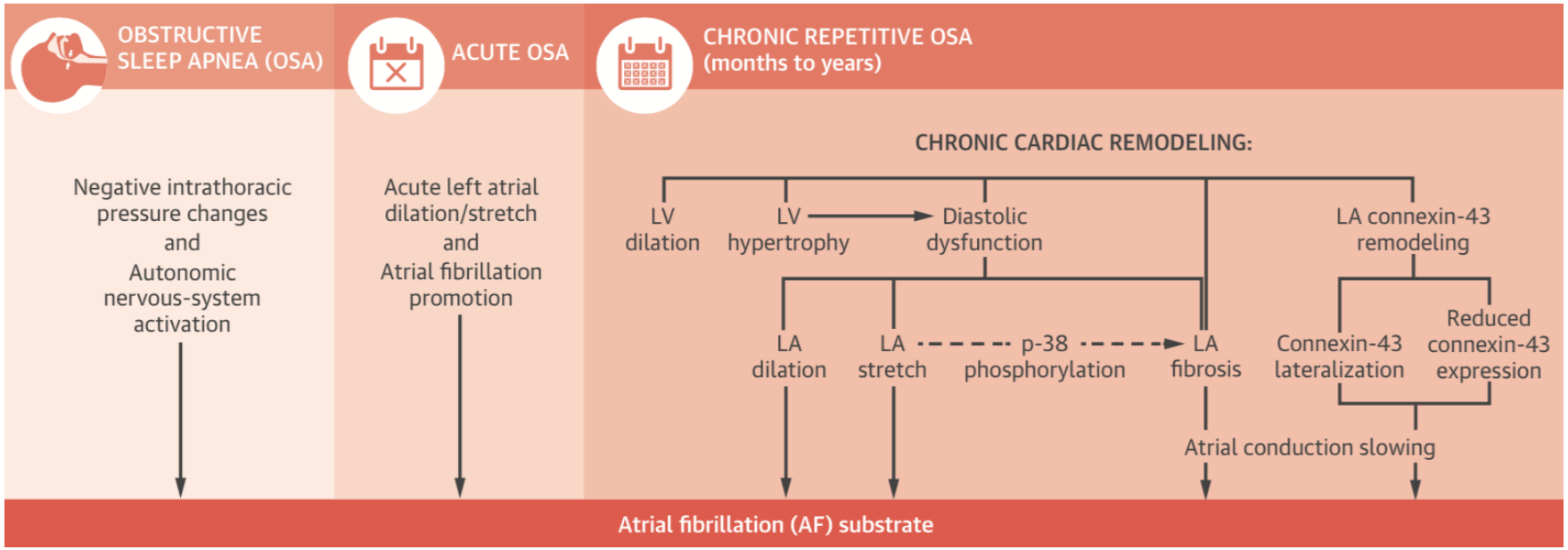
Chronic effects mediated by remodeling of the atria

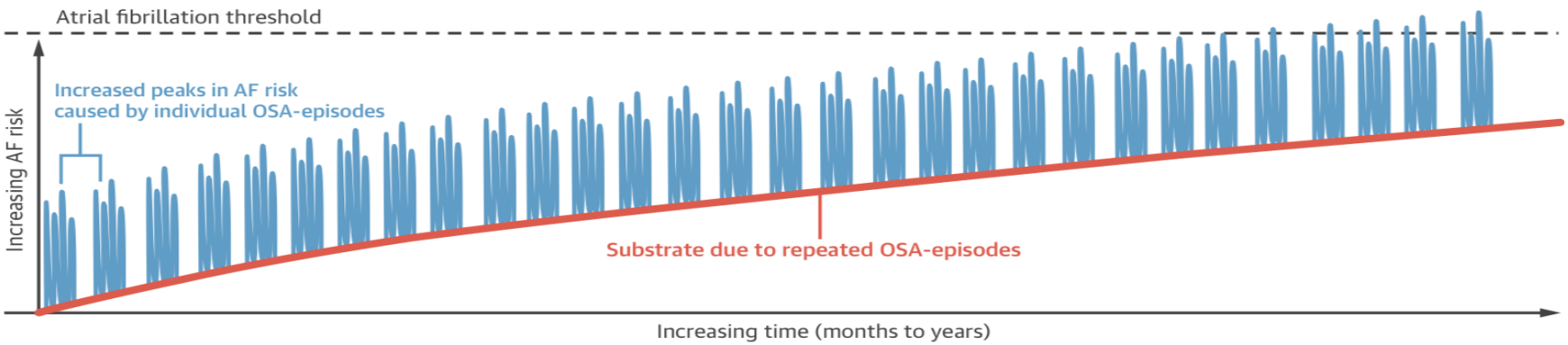




Iwasaki Yu-Ki, JACC 2014

Mechanistic Relationship



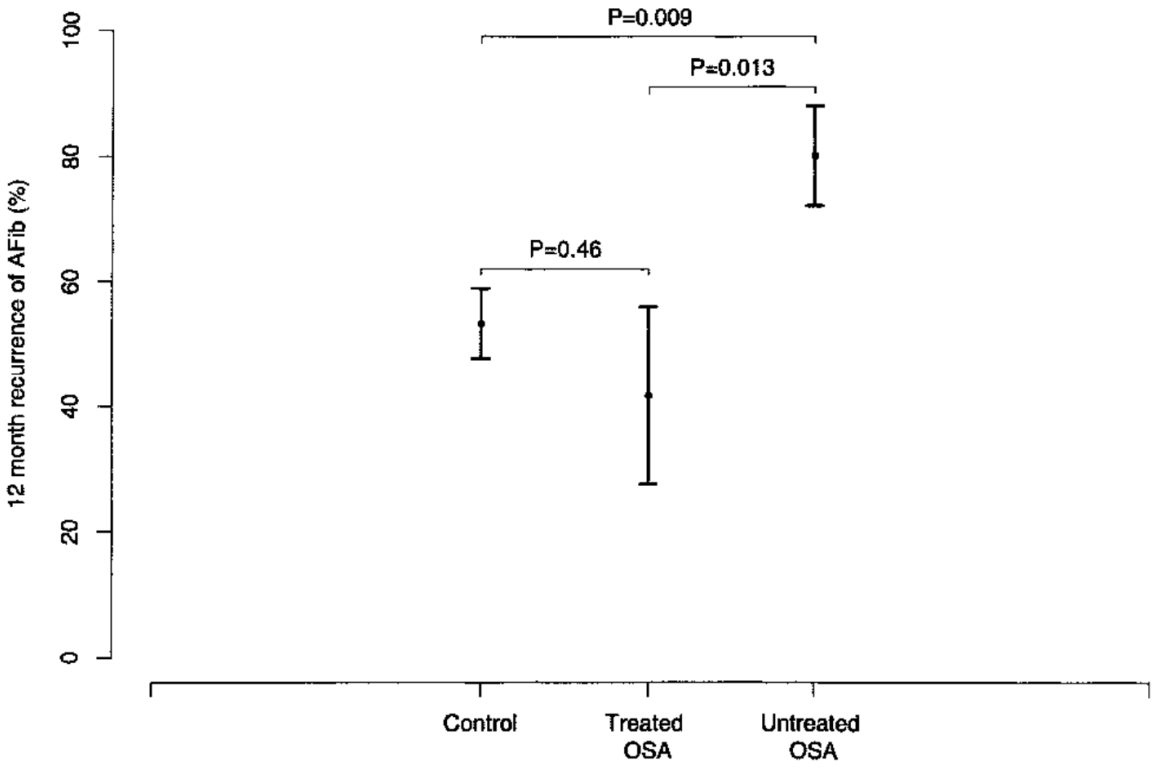


Iwasaki Yu-Ki, JACC 2014

The Effect of OSA on AF Recurrence

OSA and AF Recurrence

Patients with untreated OSA have a greater risk of AF recurrence after DCCV

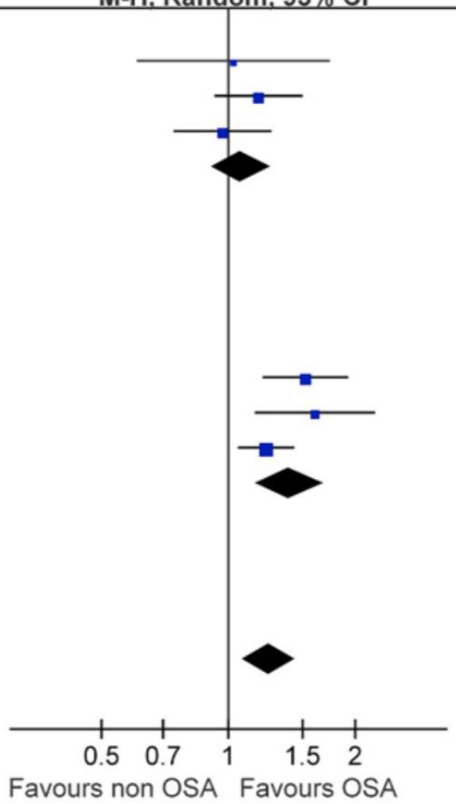


Kanagala R, Circulation 2003

OSA and AF Recurrence

Patients with OSA have a greater risk of AF recurrence after PVI

Study or Subgroup	OSA Events	OSA Total	Non OSA Events	Non OSA Total	Weight	Risk Ratio M-H, Random, 95% CI
1.1.1 Berlin Questionnaire						
Tang 2009	26	104	18	74	6.4%	1.03 [0.61, 1.73]
Chilukuri 2009	57	92	62	118	18.6%	1.18 [0.93, 1.49]
Chilukuri 2010	32	48	42	61	16.6%	0.97 [0.75, 1.26]
Subtotal (95% CI)		**244**		**253**	**41.6%**	**1.07 [0.91, 1.27]**
Total events	115		122			
Heterogeneity: Tau² = 0.00; Chi² = 1.24, df = 2 (P = 0.54); I² = 0%						
Test for overall effect: Z = 0.85 (P = 0.39)						
1.1.2 Polysomnogram						
Matiello 2010	33	42	68	132	19.1%	1.53 [1.21, 1.92]
Jongnarangsin 2008	19	32	108	292	12.9%	1.61 [1.16, 2.22]
Patel 2010	173	640	519	2360	26.4%	1.23 [1.06, 1.43]
Subtotal (95% CI)		**714**		**2784**	**58.4%**	**1.40 [1.16, 1.68]**
Total events	225		695			
Heterogeneity: Tau² = 0.01; Chi² = 4.16, df = 2 (P = 0.12); I² = 52%						
Test for overall effect: Z = 3.53 (P = 0.0004)						
Total (95% CI)		**958**		**3037**	**100.0%**	**1.25 [1.08, 1.45]**
Total events	340		817			
Heterogeneity: Tau² = 0.02; Chi² = 9.77, df = 5 (P = 0.08); I² = 49%						
Test for overall effect: Z = 3.02 (P = 0.003)						



Ng CY, Am J Card 2011

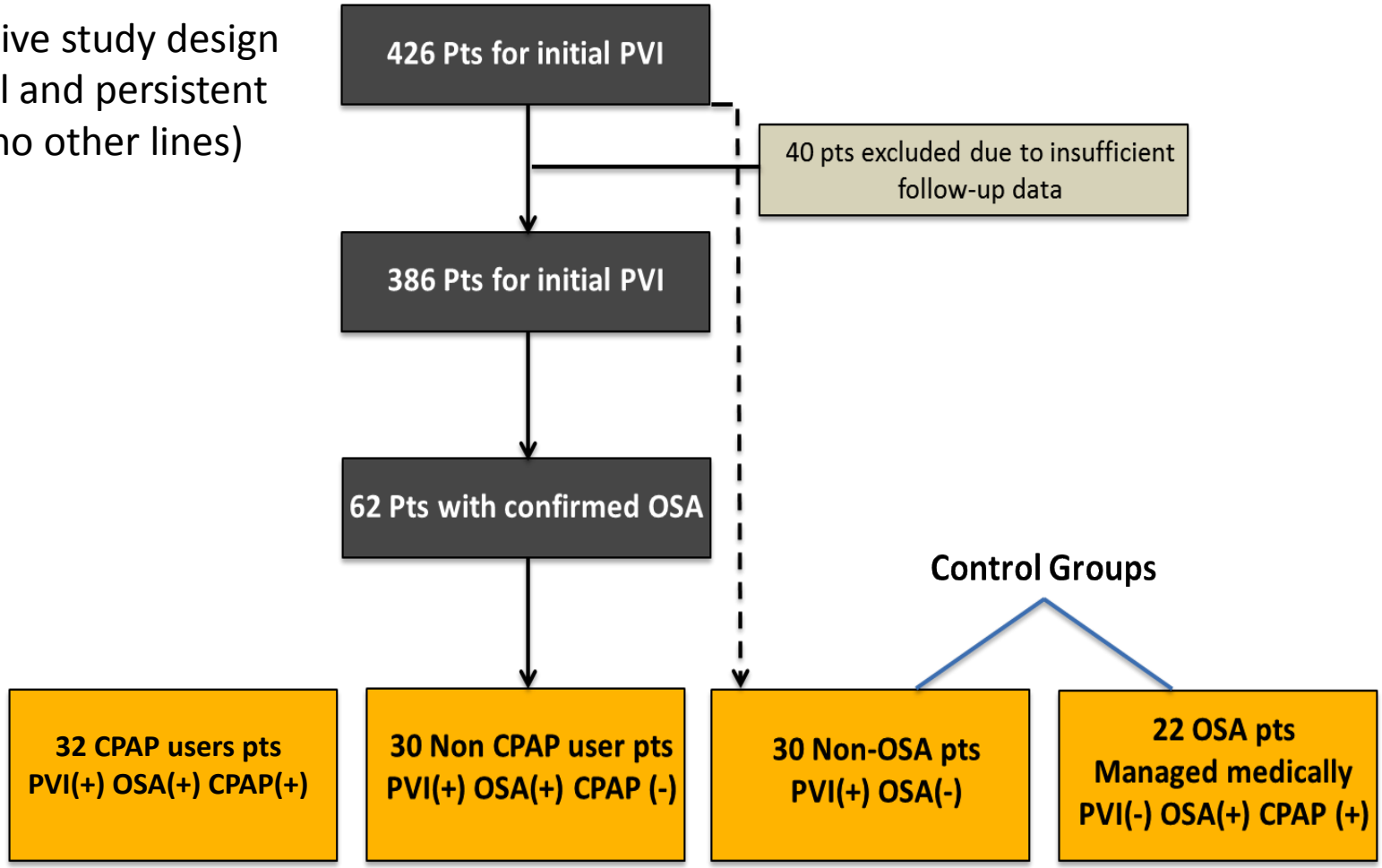
OSA and AF Recurrence

- OSA is common in patients with AF
- AF recurrence is higher in patients with OSA

Can treatment of OSA improve PVI outcome?

Effect of CPAP on PVI outcome

- Retrospective study design
- Paroxysmal and persistent
- PVI ± CTI (no other lines)



Anter E, JACC 2013

Effect of CPAP on PVI outcome

Variable	PVI (+) / OSA (+) / CPAP (+) (n=32)	PVI (+) / OSA (-) / CPAP (-) (n=30)	PVI (+) / OSA (-) / CPAP (-) (n=30)	PVI (-) / OSA (+) / CPAP (+) (n=22)	p-value
Age (years), M ±SE	56.8 ± 1.2	58.5 ± 1.4	58.5 ± 1.4	55.0 ± 1.6	0.27
Gender n, (% Male)	23 (76.7)	23 (71.9)	23 (71.9)	16 (72.7)	0.96
BMI (kg/m2), M±SE	28.77 ± 0.45	29.58 ± 0.40	29.58 ± 0.40	30.69 ± 0.99	0.11
Persistent AF n, (%)	17 (56.7)	16 (50.0)	16 (50.0)	12 (54.5)	0.95
Hypertension, n (%)	21 (70.0)	21 (65.6)	21 (65.6)	15 (68.2)	0.81
Diabetes, n (%)	6 (20.0)	6 (18.6)	6 (18.6)	4 (18.2)	1.00
CAD, n (%)	8 (26.7)	6 (18.6)	6 (18.6)	5 (22.7)	0.88
LVEF (%), M±SE	60.2 ± 1.5	59.5 ± 0.94	59.5 ± 0.94	59.3 ± 2.0	0.96
LAD(mm), M±SE	54.5 ± 0.91	55.9 ± 1.1	55.9 ± 1.1	-----	0.51*
# AAD, M±SE	1.47 ± 0.12	1.34 ± 0.10	1.34 ± 0.10	1.00 ± 0.15	0.07

Anter E, JACC 2013

Effect of CPAP on PVI outcome

Results:

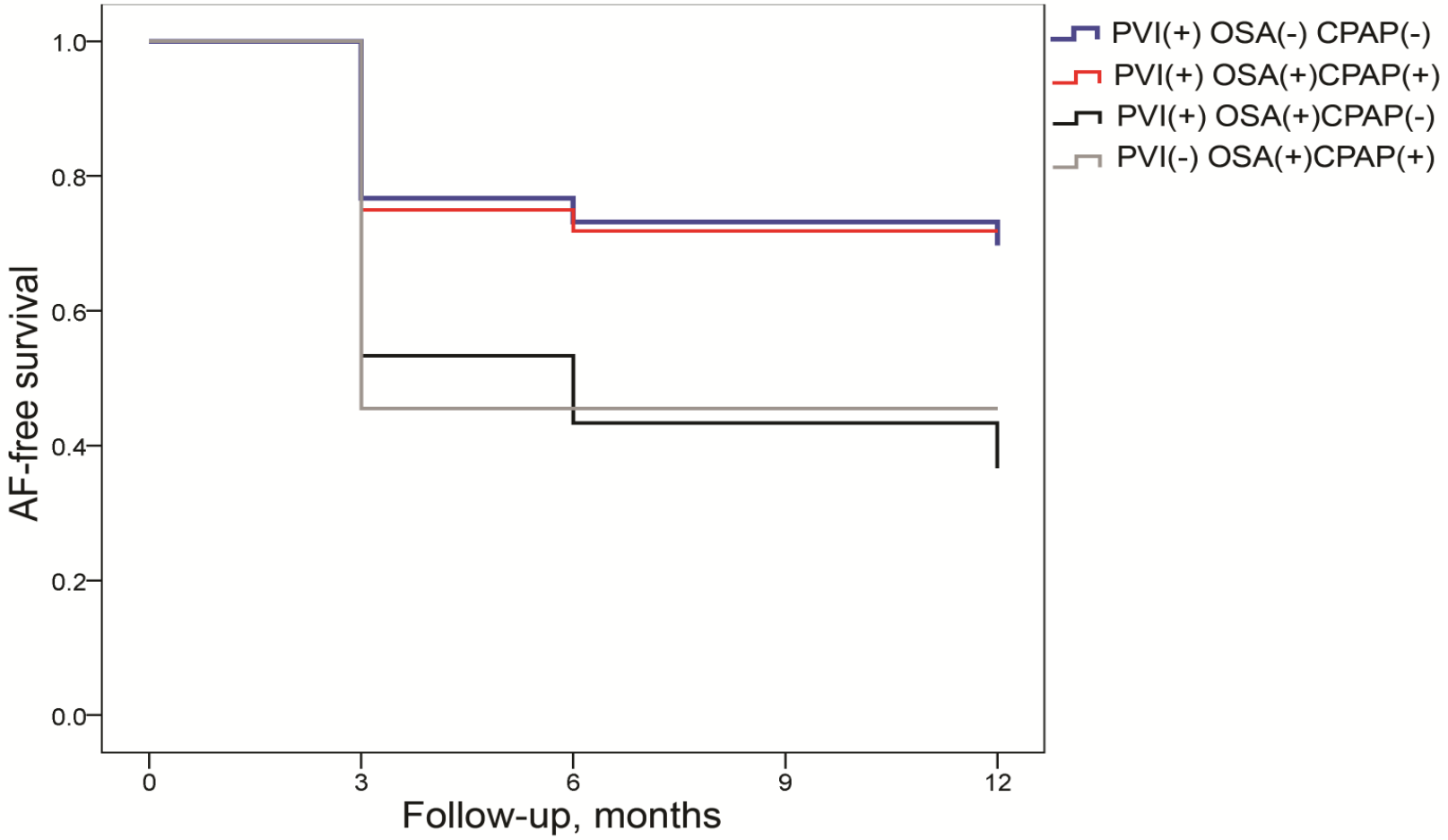
- Freedom from AF after PVI was higher in CPAP users compared with the CPAP non-users
  71.9% vs. 36.7%; p=0.01

- Patients with treated OSA had similar outcome to that of patients without OSA (p=0.94)

- Patients with untreated OSA who underwent PVI had outcome that was similar to that of patients who did not undergo PVI at all (~40%; p=0.56).

Anter E, JACC 2013

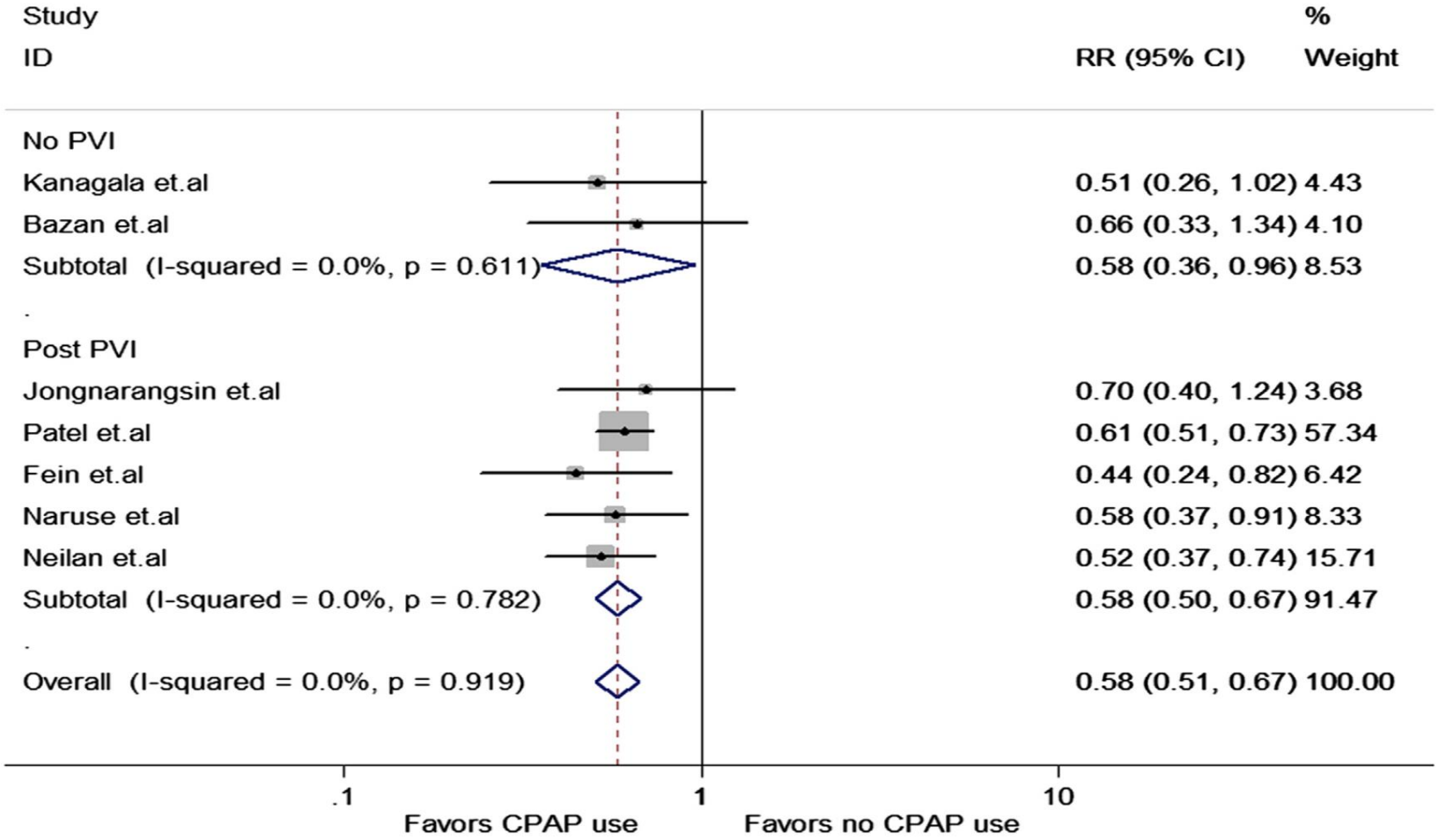
Effect of CPAP on PVI outcome



Anter E, JACC 2013

Effect of CPAP on PVI outcome

FIGURE 3 AF Recurrence in Users Versus Nonusers of CPAP in 2 Groups of Patients With OSA: PVI and Non-PVI Groups



Shukla; JACC EP 2015

Atrial Substrate in patients with PAF and OSA

Atrial Substrate and Triggers of Paroxysmal Atrial Fibrillation in Patients with Obstructive Sleep Apnea

Elad Anter, MD, **Luigi Di Biase**, MD, PhD, Eran Leshem, MD, Fernando M. Contreras-Valdes, MD, **Juan Viles-Gonzales**, MD, Alfred E. Buxton, MD, Guy Kulbak, MD, Rim N. Halaby MD, Robert J. Thomas, MD, MMSc, **Andrea Natale**, MD, **Mark E. Josephson**, MD

- Prospective, multi-center study design
- N= 172 patients
- Aimed to characterize the atrial substrate in patients with PAF and OSA:
  - Voltage distribution, electrograms, and conduction properties
  - Frequency and distribution of AF triggers
  - Role of extra-PV triggers on long-term arrhythmia control

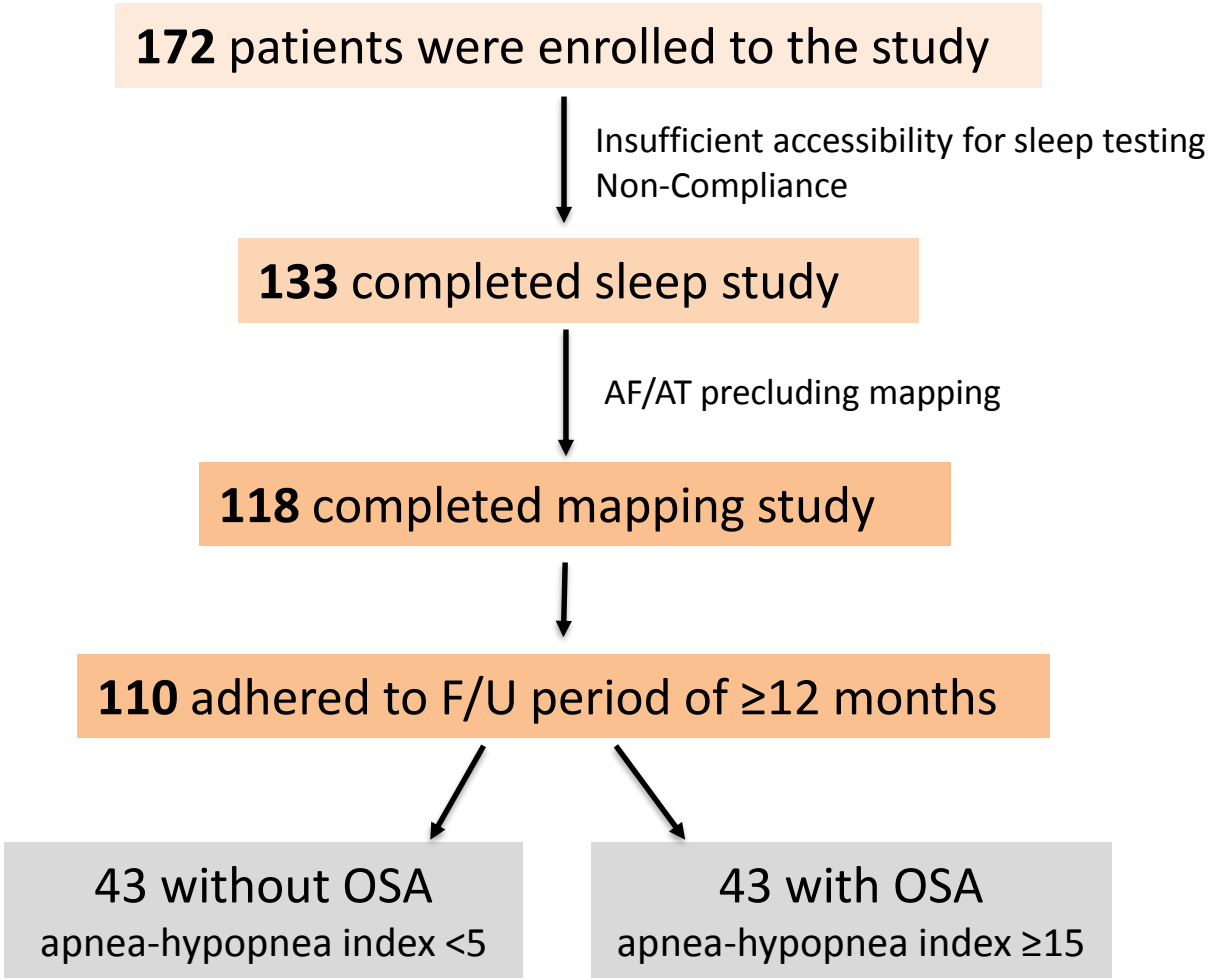
Accepted for publication Circulation A&E 2017

Atrial Substrate and Triggers of Paroxysmal Atrial Fibrillation in Patients with Obstructive Sleep Apnea

Patient population:

- Patients with symptomatic PAF without known sleep apnea presenting for first PVI
- All patients underwent sleep study before (≤ 30d) or after (≤ 90d) the ablation procedure
- In attempt to evaluate the atrial substrate specific for sleep apnea, patients with CAD, CHF, significant valvular abnormality, untreated hypertension or diabetes were excluded
- To evaluate the baseline atrial substrate and avoid measurements related to acute electrical remodeling, only patients presented in sinus rhythm were included

Atrial Substrate and Triggers of Paroxysmal Atrial Fibrillation in Patients with Obstructive Sleep Apnea



Atrial Substrate in patients with PAF and OSA

Methods:

- RA mapping was performed during pCS pacing (600-800ms)
- LA mapping was performed during dCS pacing
- Triggers of AF were determined *before* and *after* PVI

  AF triggers defined as: *APC's initiating sustained AF*
- Isoproterenol infusion with or w/o adenosine, CV during isoproterenol
- Trigger localization was estimated based on the earliest activation site, and pattern of activation from multiple left and right atrial catheters
- Triggers were ablated, followed by repeated provocation until elimination
- Follow-up duration of 12 months

Atrial Substrate and Triggers of Paroxysmal Atrial Fibrillation in Patients with Obstructive Sleep Apnea

172 patients were enrolled to the study

↓

133 completed sleep study

↓

118 completed mapping study

↓

110 adhered to 1 F/U period of 12 months

↓

43
[+PVI] [+OSA] [+Triggers]

43 with OSA
[+PVI] [-OSA] [+Triggers]

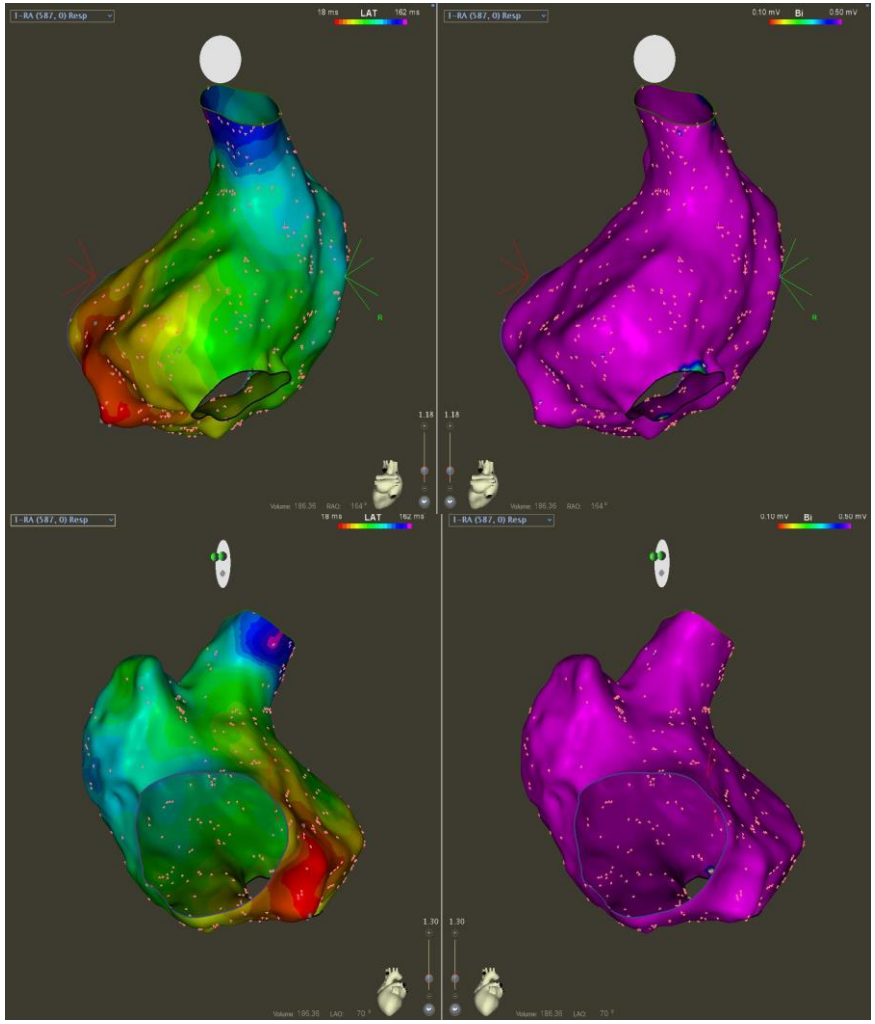
↔

50 with OSA
[+PVI] [+OSA] [-Triggers]

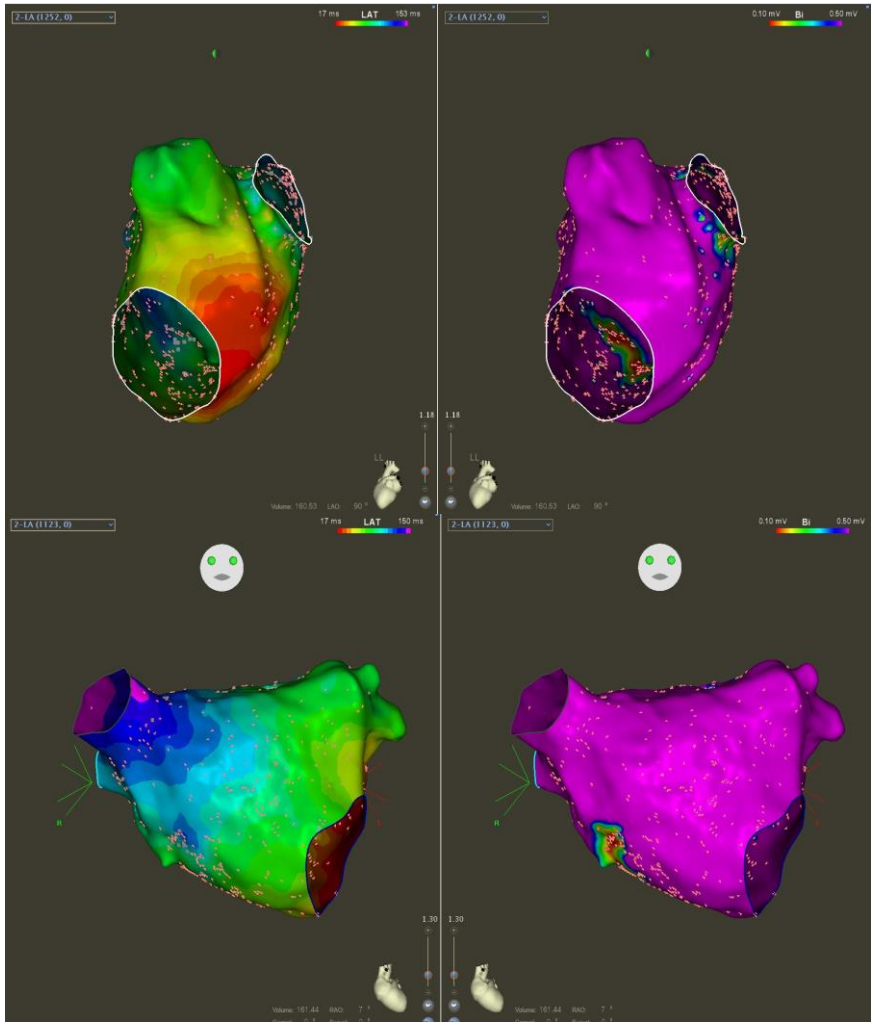
48 without OSA
[-PVI] [+OSA] [-Triggers]

Atrial Substrate in patients with PAF without OSA

Right Atrium

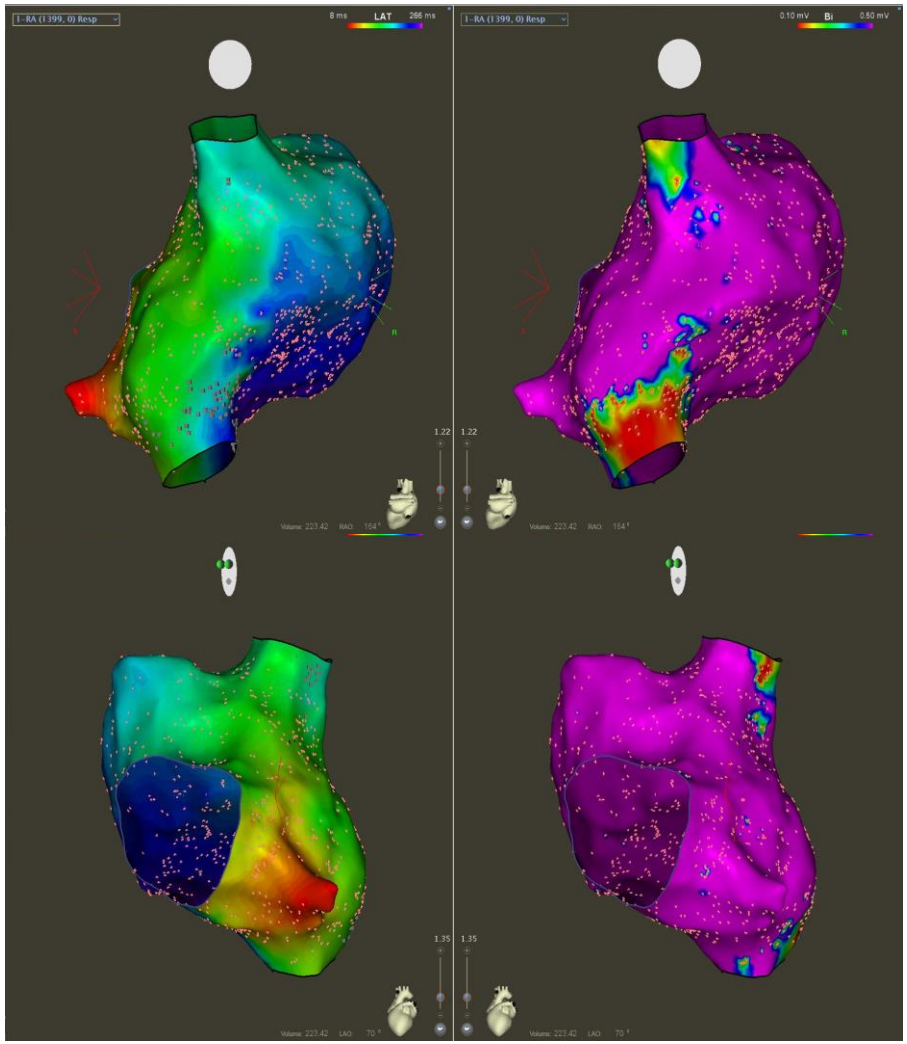


Left Atrium

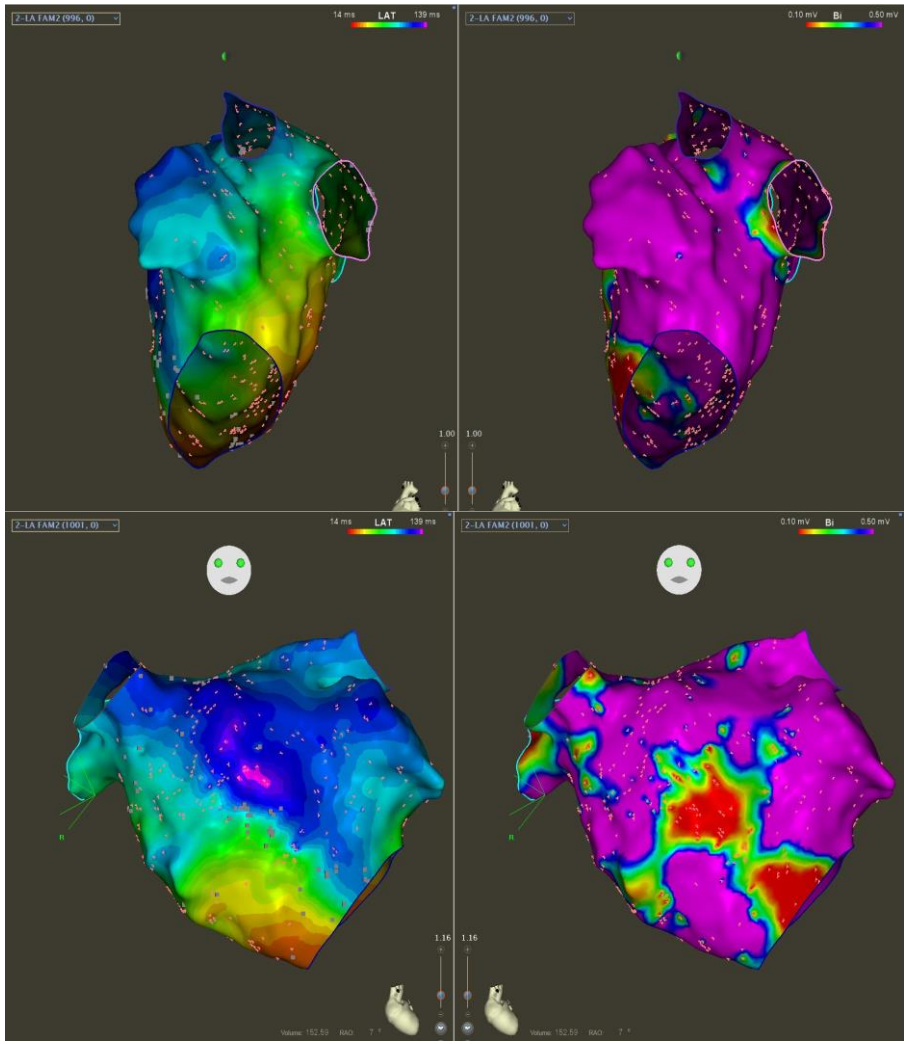


Atrial Substrate in patients with PAF and OSA

Right Atrium

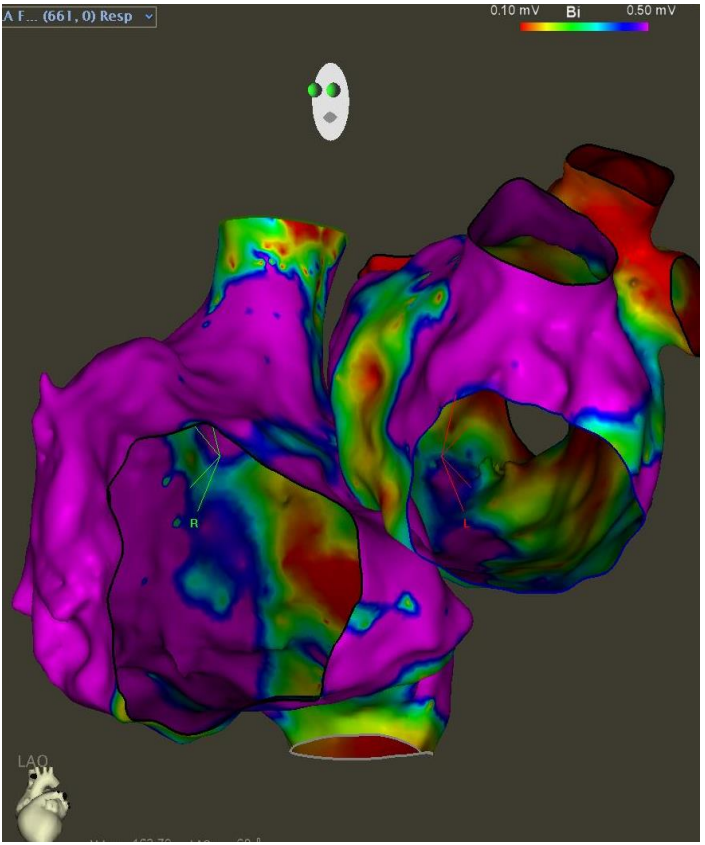


Left Atrium



Atrial Substrate in patients with PAF and OSA

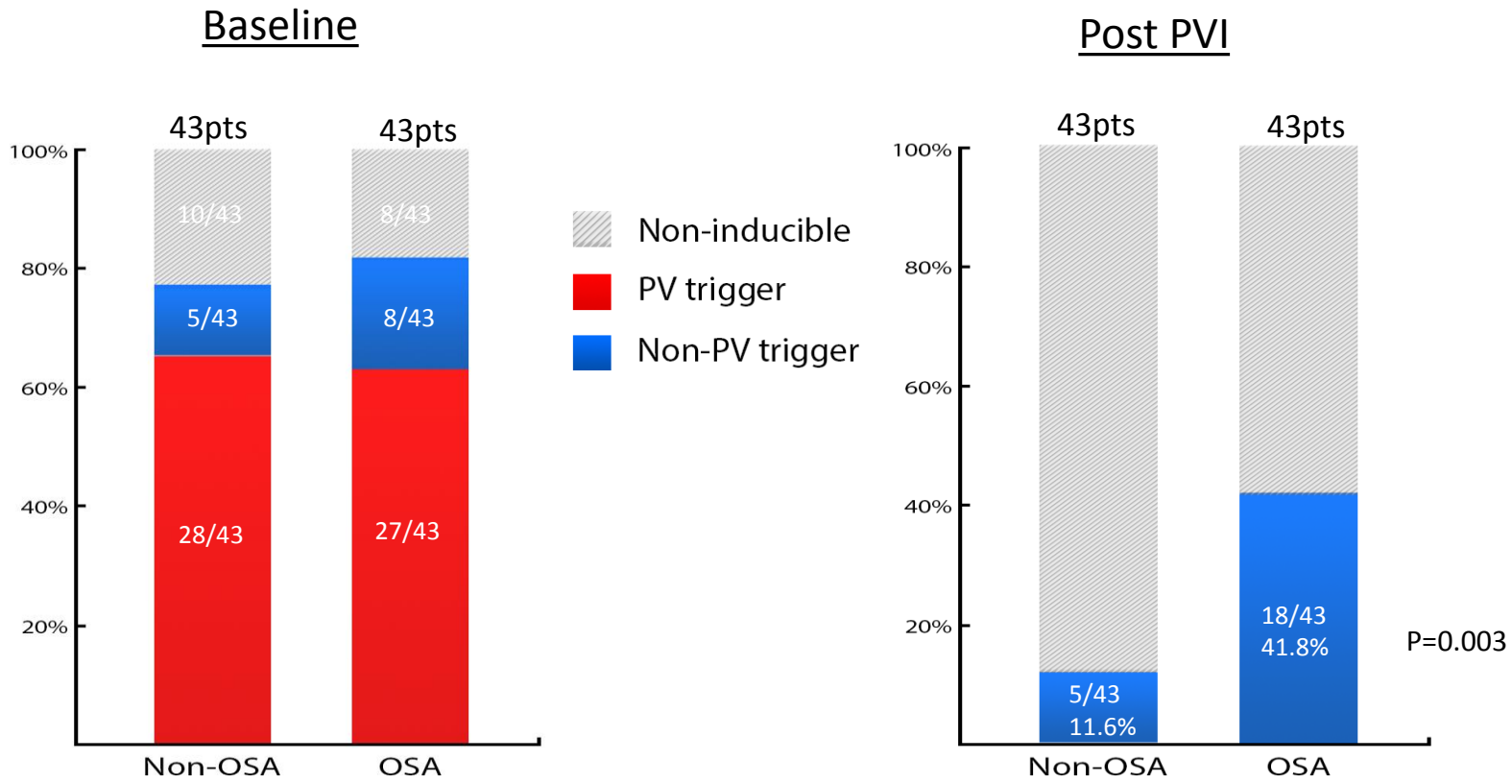
Biatrial Voltage Map



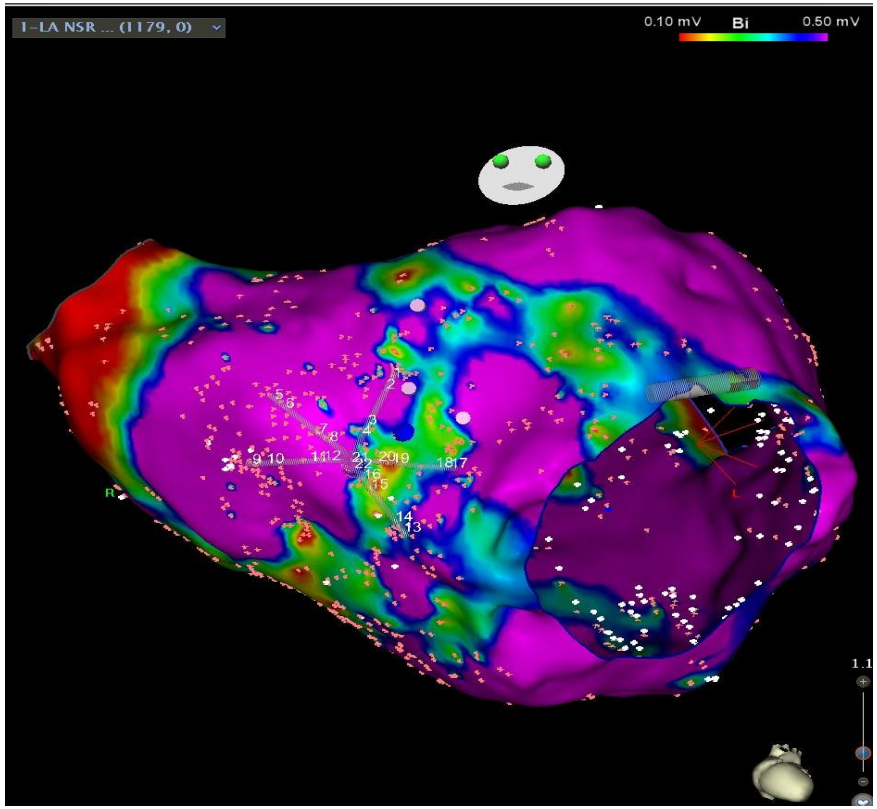
Right Atrial Septum EGM

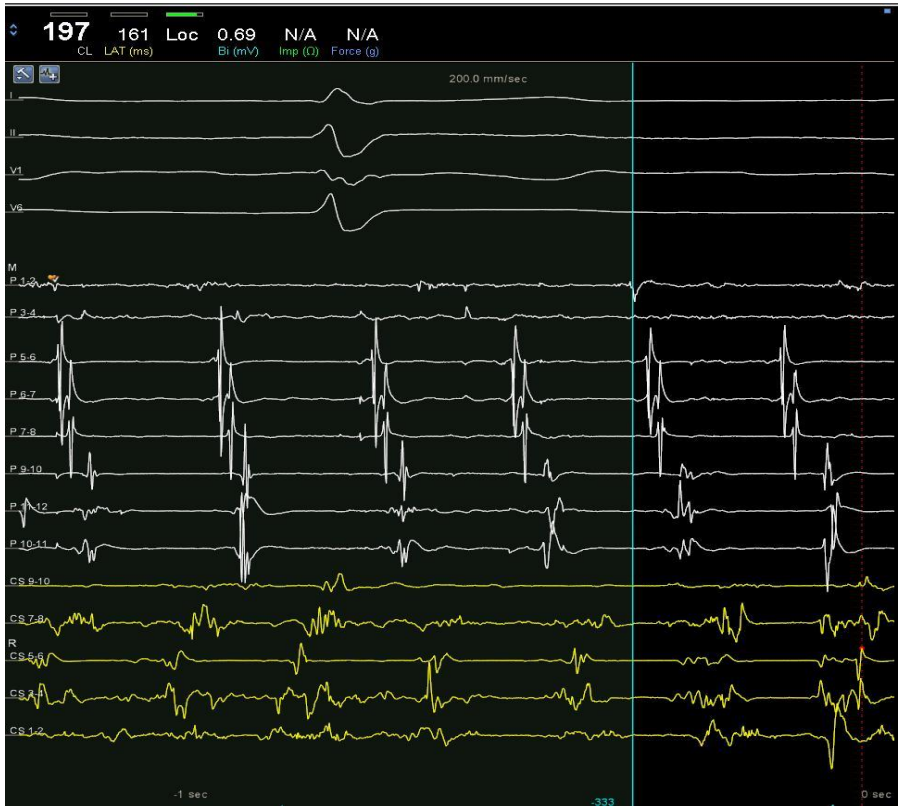
Left Atrial Septum EGM

Triggers of AF in patients with OSA

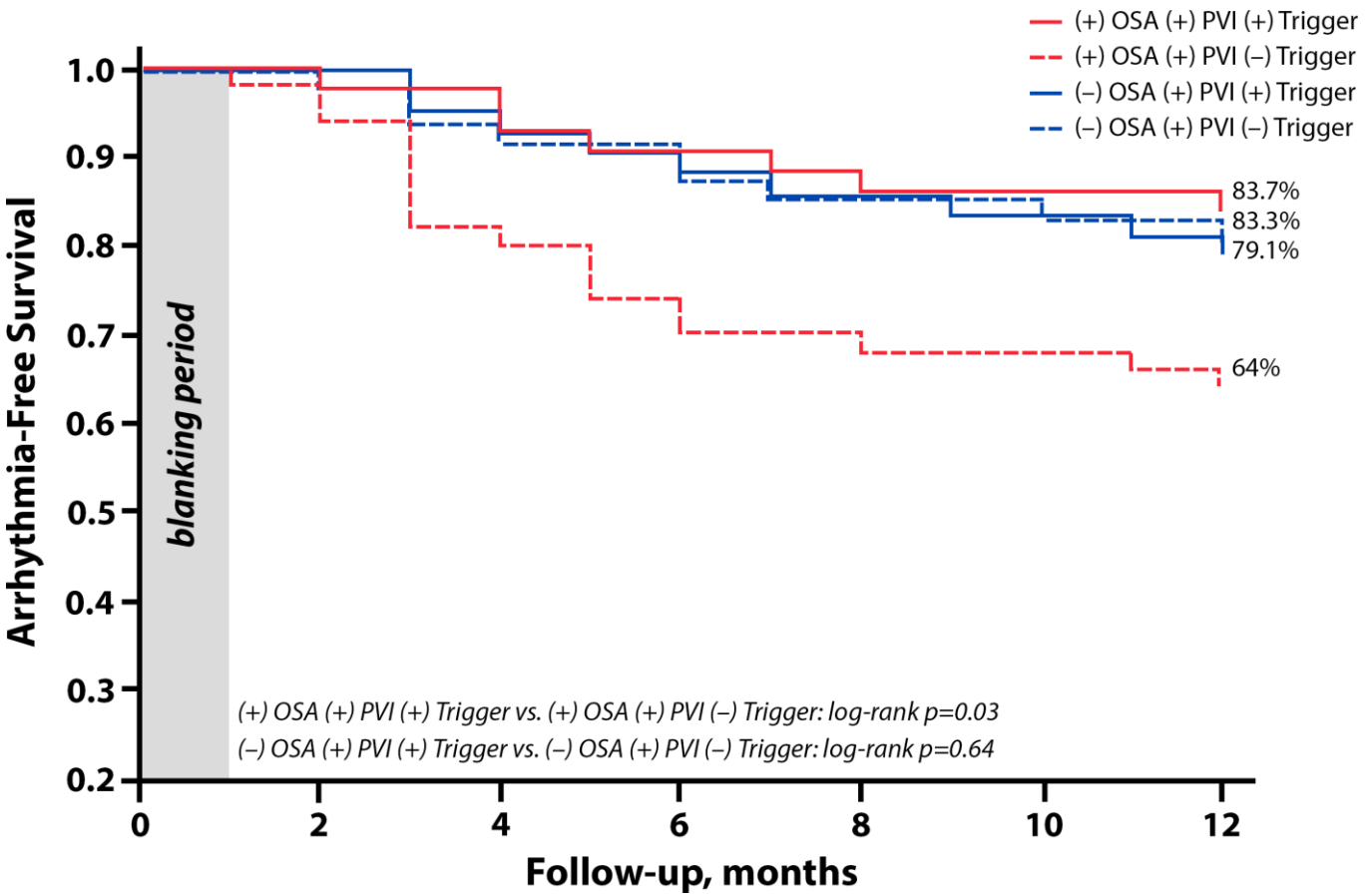


Scar as anchor for rotational activity in OSA





Clinical outcome of Extra-PV trigger ablation



Summary and Future directions

- Growing body of evidence implicating sleep apnea in atrial remodeling and promotion of the AF substrate
- Changes are both substrate and trigger-based
- PAF in patients with OSA is often associated with areas of low voltage and slow conduction, predominantly affecting the left anterior septum
- These zones are a common source of extra-PV triggers and localized circuits (rotors) of AF
- Ablation of these low voltage zones is associated with improved clinical outcome in patients with PAF and OSA.
- PVI alone (even in patients with PAF) may not be sufficient, and at the least requires evaluation of extra PV triggers

Summary and Future directions

However…

- Similar phenotype can be observed in patients without sleep apnea (often in persistent AF), such that sleep apnea may act as a facilitator rather than a cause.

- In the meantime, patients with AF should at least be screened for OSA as part of a wider approach for cardiovascular and AF risk reduction (i.e., ARREST-AF)

- Data on AF and OSA are largely observational. There is an urgent need for randomized trails to evaluate the impact of sleep apnea and its therapy on cardiovascular risk reduction

- Prevention and early diagnosis may be better than treatment of advanced disease (it may explain discrepancies in respond to Rx)

SLA-AF

SLeep Apnea Management after AF ablation

- Prospective randomized controlled multicenter study in 600 pts
- Patients with AF referred for ablation with a positive Watchpat sleep study (AHI ≥15)
- 1:1 randomization to either to catheter ablation (control arm) or catheter ablation + OSA therapy (treatment arm).
- 1st end-point: single procedure freedom from AF off AADs at 1y
- 2nd end-point: changes in endothelial function, and atrial size 1yr

Elad Anter, Vivek Reddy

The BIDMC Approach

CardioVascular Institute
at Beth Israel Deaconess Medical Center

Cardiology – Sleep Medicine Program

Appointments: 617-667-8800
bidmc.org/cardsleep

Beth Israel Deaconess Medical Center
HARVARD MEDICAL SCHOOL TEACHING HOSPITAL

Welcome

Our multidisciplinary Cardiology – Sleep Medicine Program offers people with atrial fibrillation screening for sleep apnea as part of their cardiology care. Follow-up care is provided by our sleep medicine team.

Sleep Apnea and the Heart

- Sleep apnea is common in the general population, affecting approximately 42 million Americans.
- Sleep apnea is common in patients with heart disease, especially those with cardiac arrhythmias.
- About 50% of people with sleep apnea have not been diagnosed.
- Diagnosis and treatment can improve heart health and overall well-being.

What is sleep apnea?

A common disorder in which pauses in breathing or shallow breathing disrupts sleep.

What is atrial fibrillation?

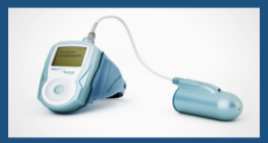
An irregular heartbeat caused by disorganized beating of the upper heart chambers. Though rarely life-threatening, it can cause stroke and increase the risk of heart failure.

What is an ablation?

A procedure in which an electrophysiologist uses energy (usually radiofrequency) to make small scars in the heart tissue to prevent abnormal electrical signals from moving through the heart.

How do we know there is an association between sleep apnea and atrial fibrillation?

Multiple scientific studies in recent years have documented this connection.

Do You Have Sleep Apnea?

As part of your treatment, you will receive a small, wrist-mounted diagnostic device that is easy to operate. Its fast, accurate results make this home sleep test equivalent to sleep-lab testing.