KHRS 2021 VIRTUAL

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대한부정맥학회

Korean Heart Rhythm Society

Implication of Sleep Apnea in The Management of Atrial Fibrillation

Younghoon Kwon, MD

Division of Cardiology

Section of Sleep Medicine, Division of Pulmonary Critical Care

University of Washington

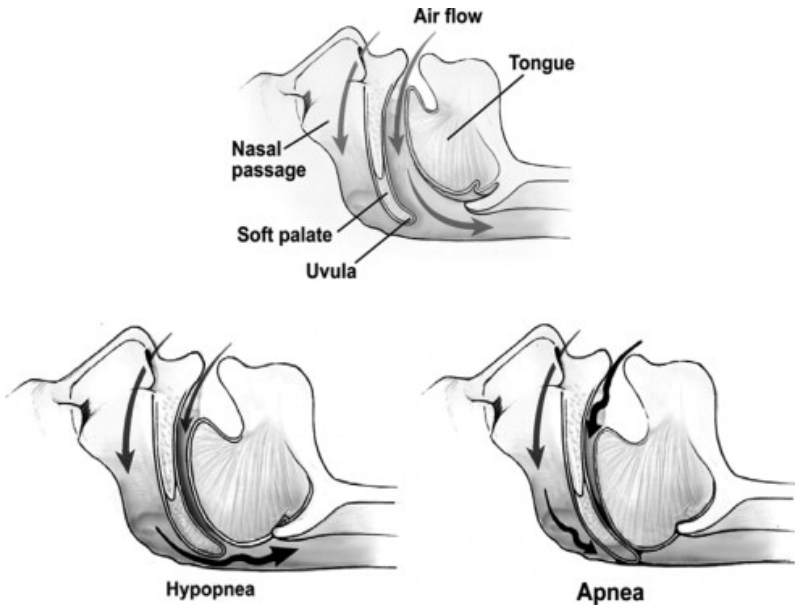
- Disclosure
  - Research support: NIH, ResMed foundation

Objectives

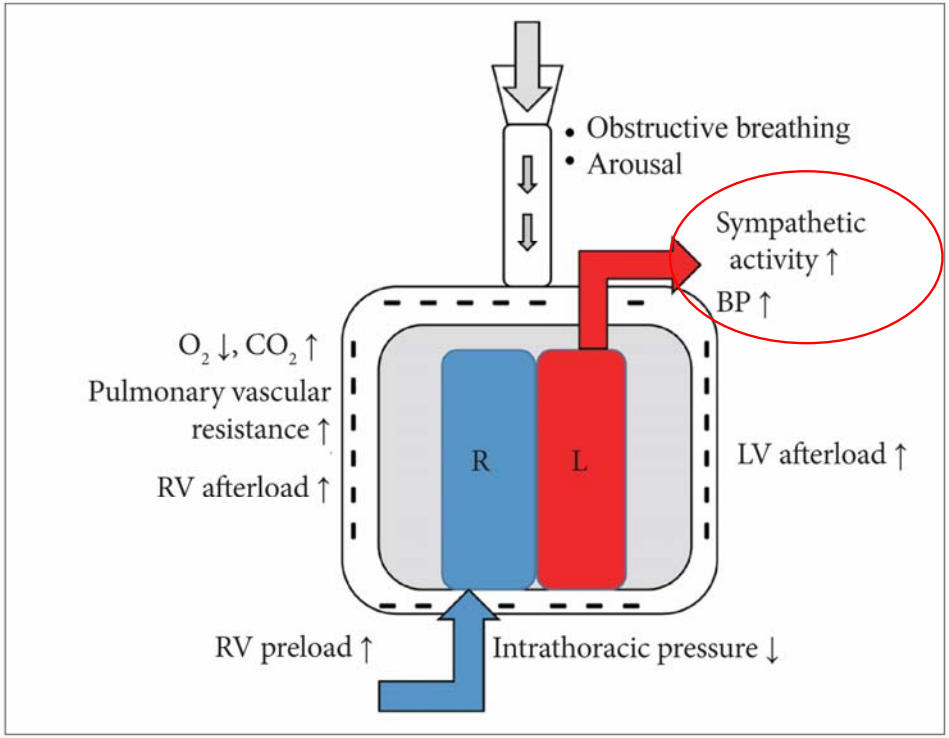
- Basics of sleep apnea (SA)
- Review of studies Re: Sleep apnea (SA) and atrial fibrillation (AF)
- Challenges and future prospects on SA-AF

Obstructive sleep apnea (OSA) and CVD

- OSA very common (spectrum)
- OSA increases the CV risks/CVD/ mortality
  - Hypertension / resistant hypertension
  - Heart failure, stroke, coronary heart disease
  - AF

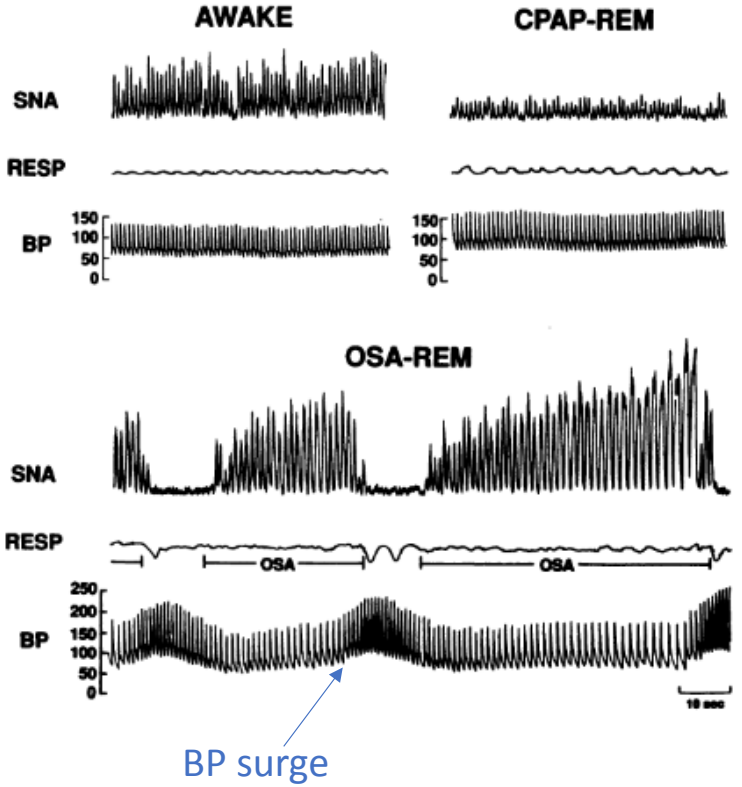


OSA event - pathophysiology



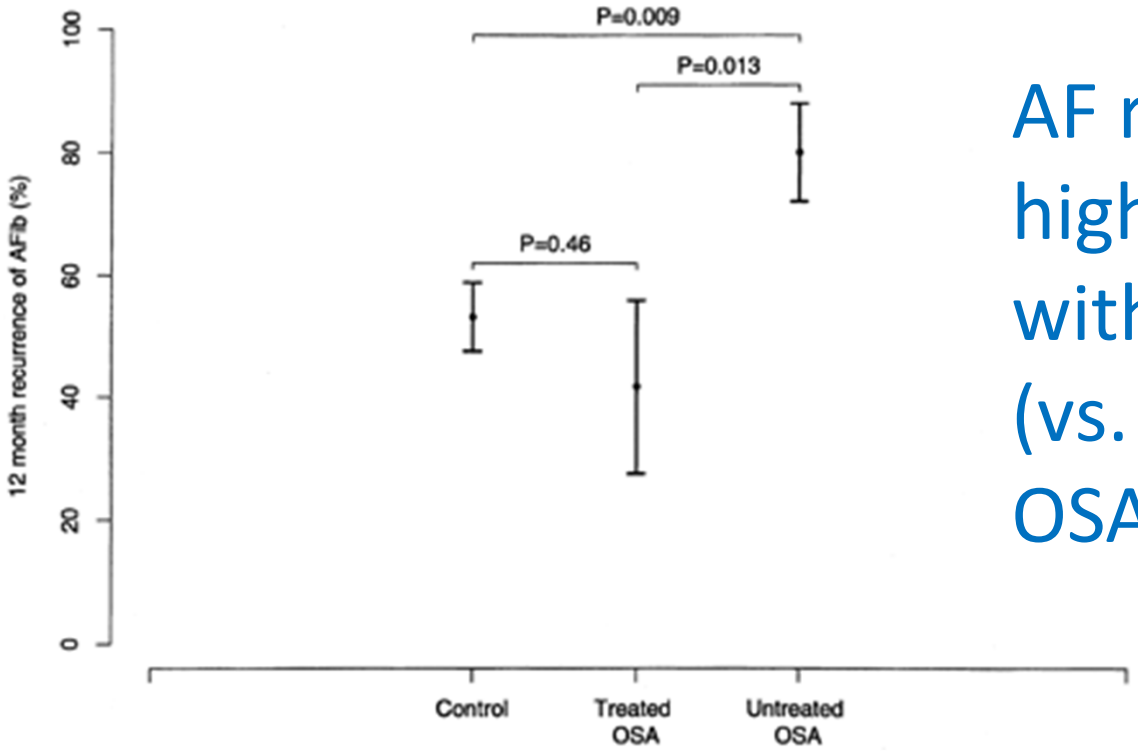
Kwon et al., (Review) Sleep Med Research 2020

SNA: sympathetic nervous activity



Somers et al., JCI 1995

AF recurrence after cardioversion



AF recurrence much higher in patients with untreated OSA (vs. control or treated OSA)

Kanagala et al. Circulation 2003

OSA and incidence of AF

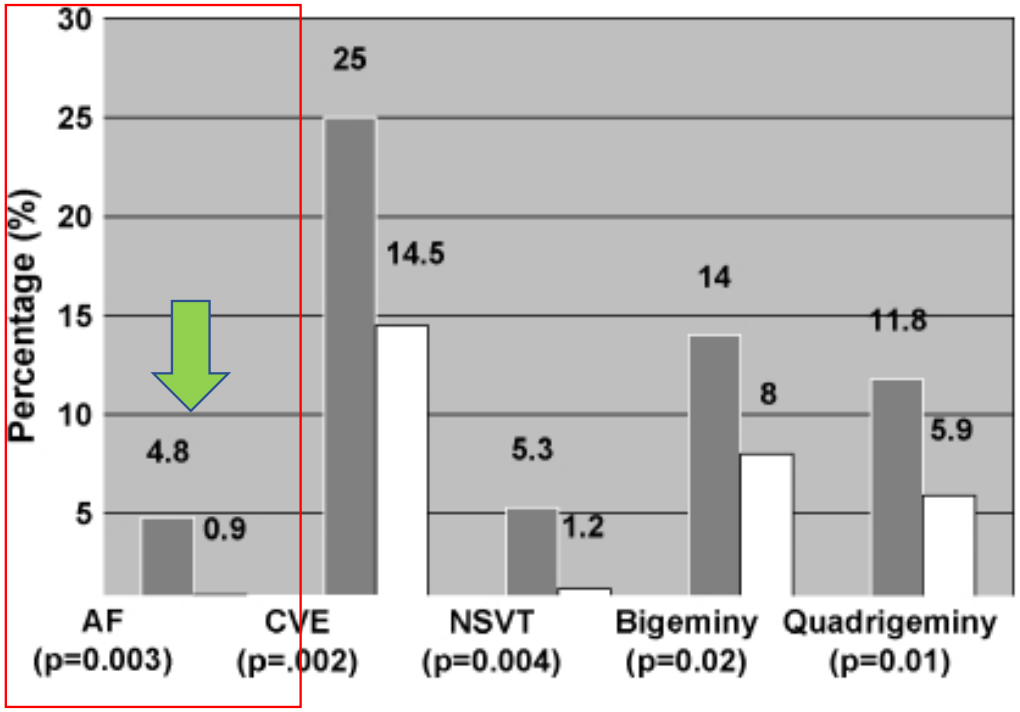
Multivariable analysis

The lower the min O2 sat at night, the higher the incidence of AF

	HR	95% CI	p Value
<65 yrs old			
Age (per 10 yrs)	2.04	1.48–2.80	<0.001
Male gender	2.66	1.33–5.30	0.006
Coronary artery disease	2.66	1.46–4.83	0.001
Body mass index (per 1 kg/m ^{2})	1.07	1.05–1.10	<0.001
Decrease in nocturnal oxygen saturation (per −1%) *	3.29	1.35–8.04	0.009
≥65 yrs old			
Heart failure	7.68	4.32–13.66	<0.001

Gami et al. JACC 2007

Nocturnal Arrhythmia (Cross sectional)

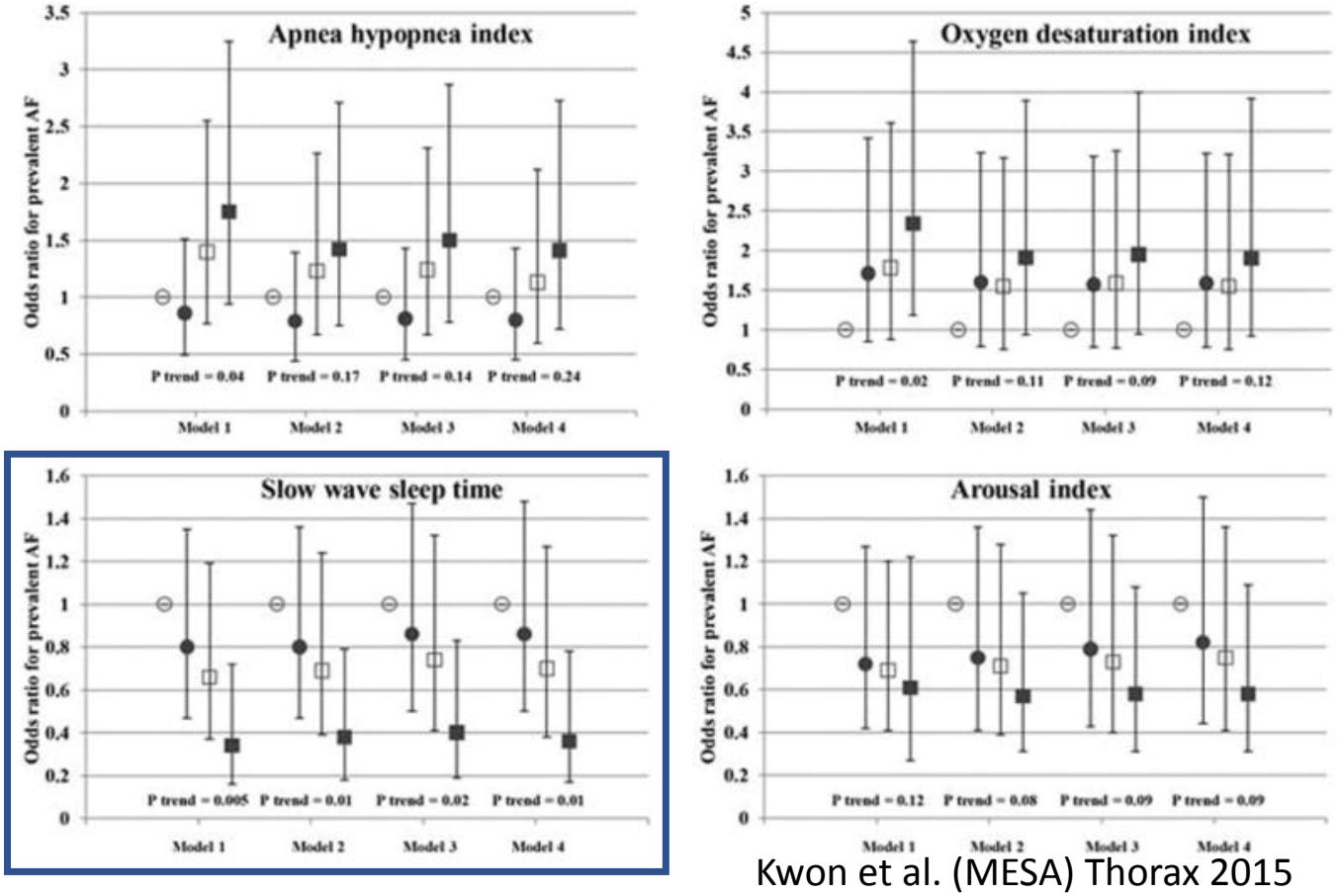


Complex ventricular ectopy (i.e., bigeminy, trigeminy, quadrigeminy, or nonsustained ventricular tachycardia)

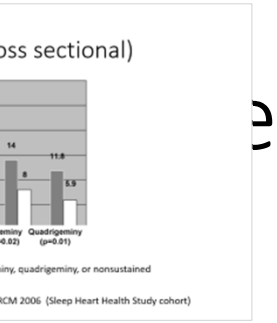
Mehra et al. AJRCM 2006 (Sleep Heart Health Study cohort)

Beyond OSA

Low slow wave sleep is associated with higher chance of having AF



Kwon et al. (MESA) Thorax 2015



entral sleep apnea and incident AF

Age ≥76 yr			
AHI per 5-unit increase	42/314	**1.20 (1.08–1.33)**	**1.22 (1.08–1.39)**
AHI <15	16/183	1.00 (reference)	1.00 (reference)
AHI ≥15	26/131	**2.91 (1.43–5.90)**	**2.64 (1.16–6.00)**
OAHI per 5-unit increase‡	42/314	**1.17 (1.05–1.30)**	1.13 (0.98–1.29)
CAI <5	35/295	1.00 (reference)	1.00 (reference)
CAI ≥5‡	7/19	**4.86 (1.72–13.72)**	**9.97 (2.72–36.50)**
No CSA-CSR	34/289	1.00 (reference)	1.00 (reference)
CSA-CSR‡	8/25	**3.88 (1.50–10.07)**	**6.31 (1.94–20.51)**

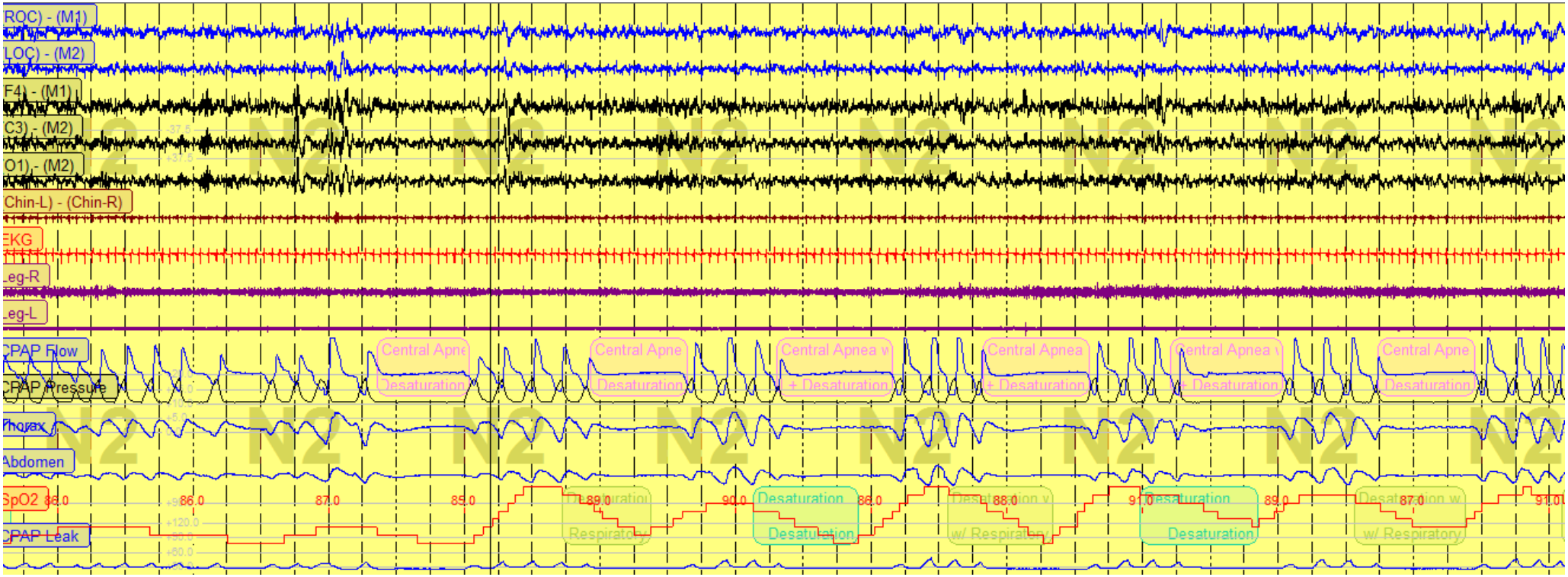
CAI: central apnea index

CSA: central sleep apnea

CSR: Cheyne Stokes Respiration

May et al. AJRCCM 2015 MrOS Sleep cohort

CSA (central sleep apnea) example (polysomnography)



Central sleep apnea and incident AF

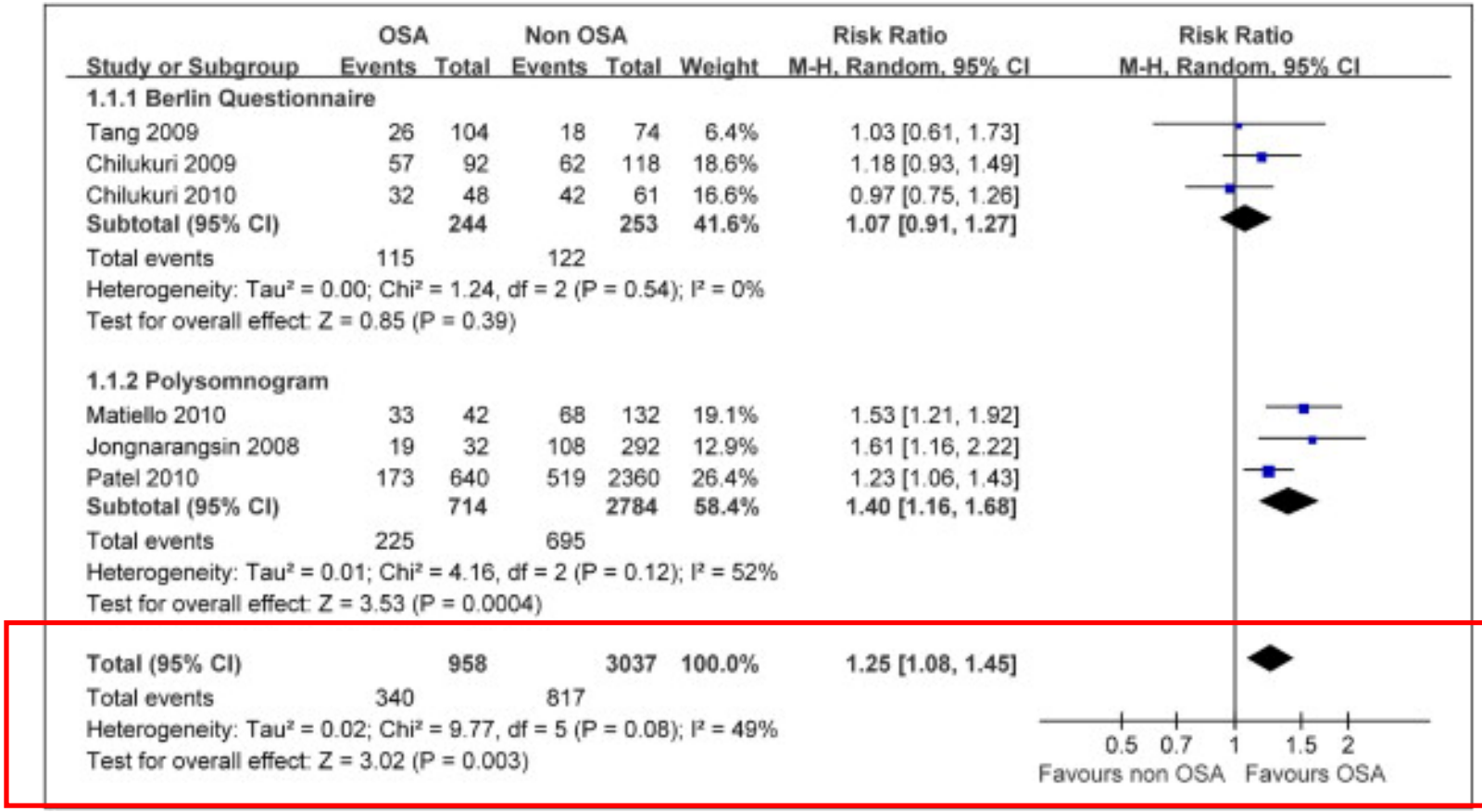
	Minimally Adjusted[a]	Multivariable Adjusted[b]	Multivariable Adjusted[b]+OAHI	Multivariable Adjusted[b]+CAI
OAHI, per 5 increase	0.97 (0.91–1.02), 0.22	0.97 (0.91–1.03), 0.26	NA	0.96 (0.90–1.02), 0.21
OAHI <5 (reference)	1.00 (reference)	1.00 (reference)	NA	1.00 (reference)
OAHI 5 to <15	0.79 (0.58–1.08), 0.14	0.84 (0.59–1.17), 0.30	NA	0.81 (0.58–1.14), 0.23
OAHI 15 to <30	0.91 (0.61–1.36), 0.65	0.93 (0.60–1.45), 0.75	NA	0.91 (0.59–1.42), 0.69
OAHI ≥30	0.78 (0.47–1.32), 0.36	0.76 (0.42–1.36), 0.35	NA	0.72 (0.40–1.30), 0.28
CAI ≥5	1.71 (0.89–3.30), 0.11	3.00 (1.40–6.44), 0.005	3.15 (1.46–6.80), 0.003	NA
CSR	1.77 (0.99–3.16), 0.05	1.83 (0.95–3.54), 0.07	1.92 (0.99–3.73), 0.05	NA

CAI: central apnea index

CSR: Cheyne Stokes Respiration

Tung et al. JAHA 2017 SHHS cohort

AF recurrence after PVI



Ng et al. AJC 2011

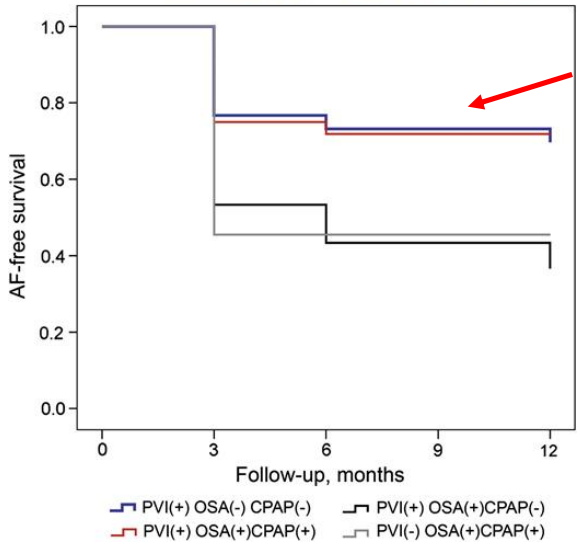
Tx of OSA and risk of AF after PVI

Journal of the American College of Cardiology
Volume 62, Issue 4, 23 July 2013, Pages 300–305

Clinical Research

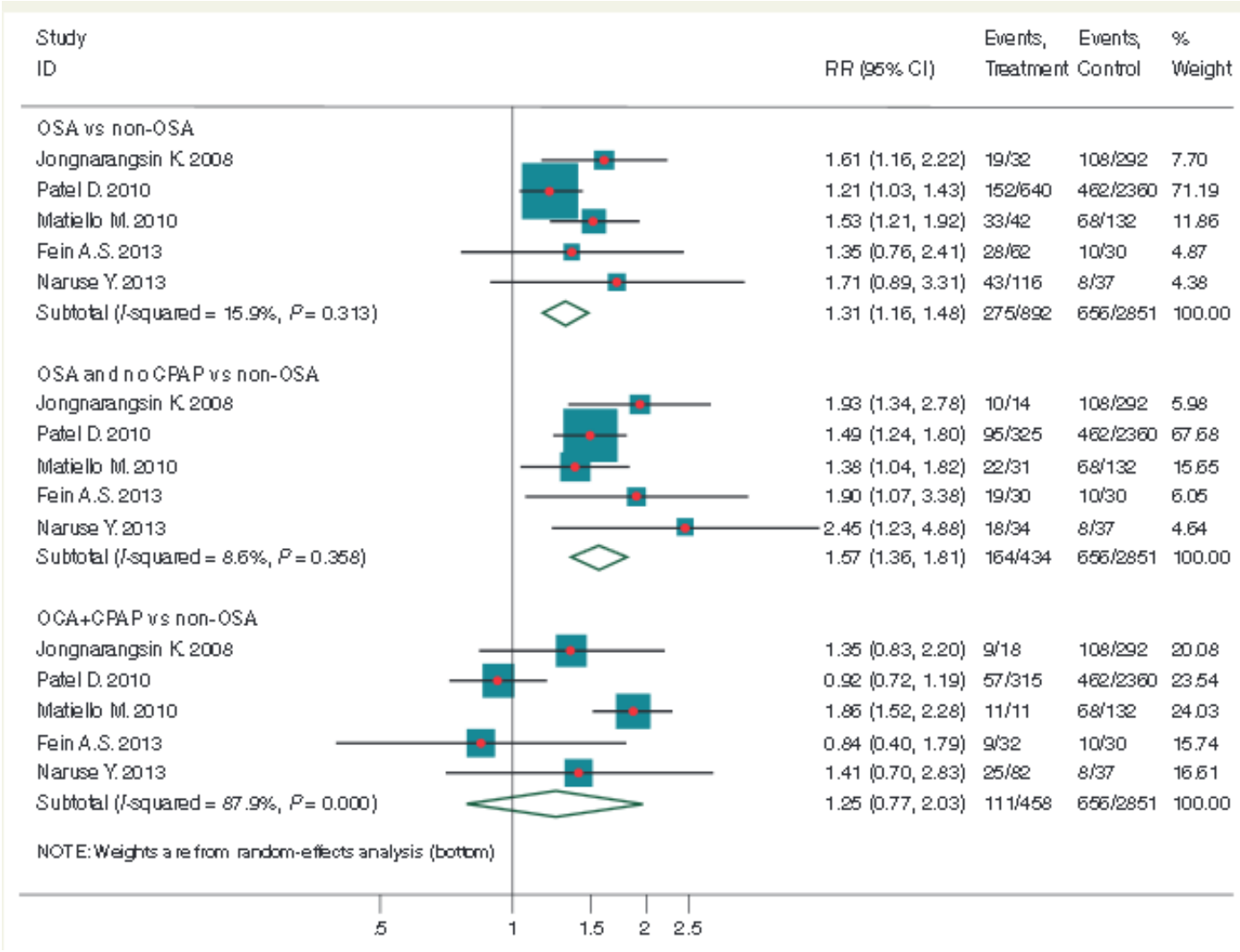
Treatment of Obstructive Sleep Apnea Reduces the Risk of Atrial Fibrillation Recurrence After Catheter Ablation

Adam S. Fein, MD, Alexei Shvilkin, MD, PhD, Dhaval Shah, MD, Charles I. Haffajee, MD, Saumya Das, MD, Kapil Kumar, MD, Daniel B. Kramer, MD, Peter J. Zimetbaum, MD, Alfred E. Buxton, MD, Mark E. Josephson, MD, Elad Anter, MD



CPAP treatment – lower recurrence of AF after ablation

Fein et al JACC 2013



Li et al. Europace 2014

Tx of OSA on AF recurrence

Effect of Obstructive Sleep Apnea Treatment on Atrial Fibrillation Recurrence

A Meta-Analysis

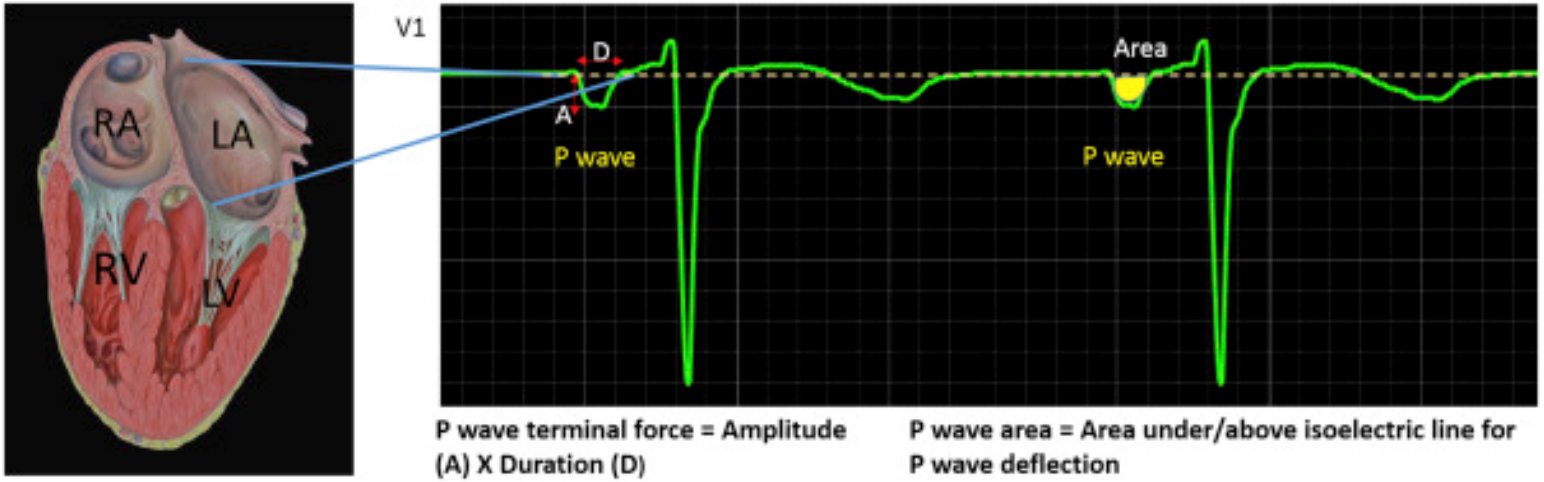
Ashish Shukla, MD, MPH; Anthony Aizer, MD, MSc; Douglas Holmes, MD; Steven Fowler, MD; David S. Park, MD, PhD; Scott Bernstein, MD; Neil Bernstein, MD; Larry Chinitz, MD

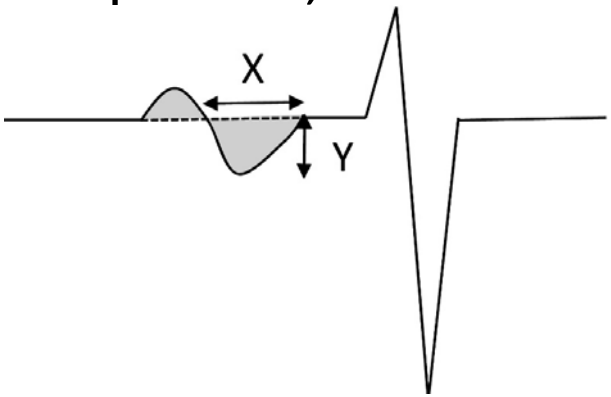
JACCCEP. 2015;1(1):41-51. doi:10.1016/j.jacep.2015.02.014

Across all patient groups, the use of CPAP was associated with a significant reduction in AF recurrence (relative risk: 0.58, 95% confidence interval: 0.51 to 0.67; heterogeneity chi-square p = 0.91, I2 = 0%).

ECG markers of LA remodeling

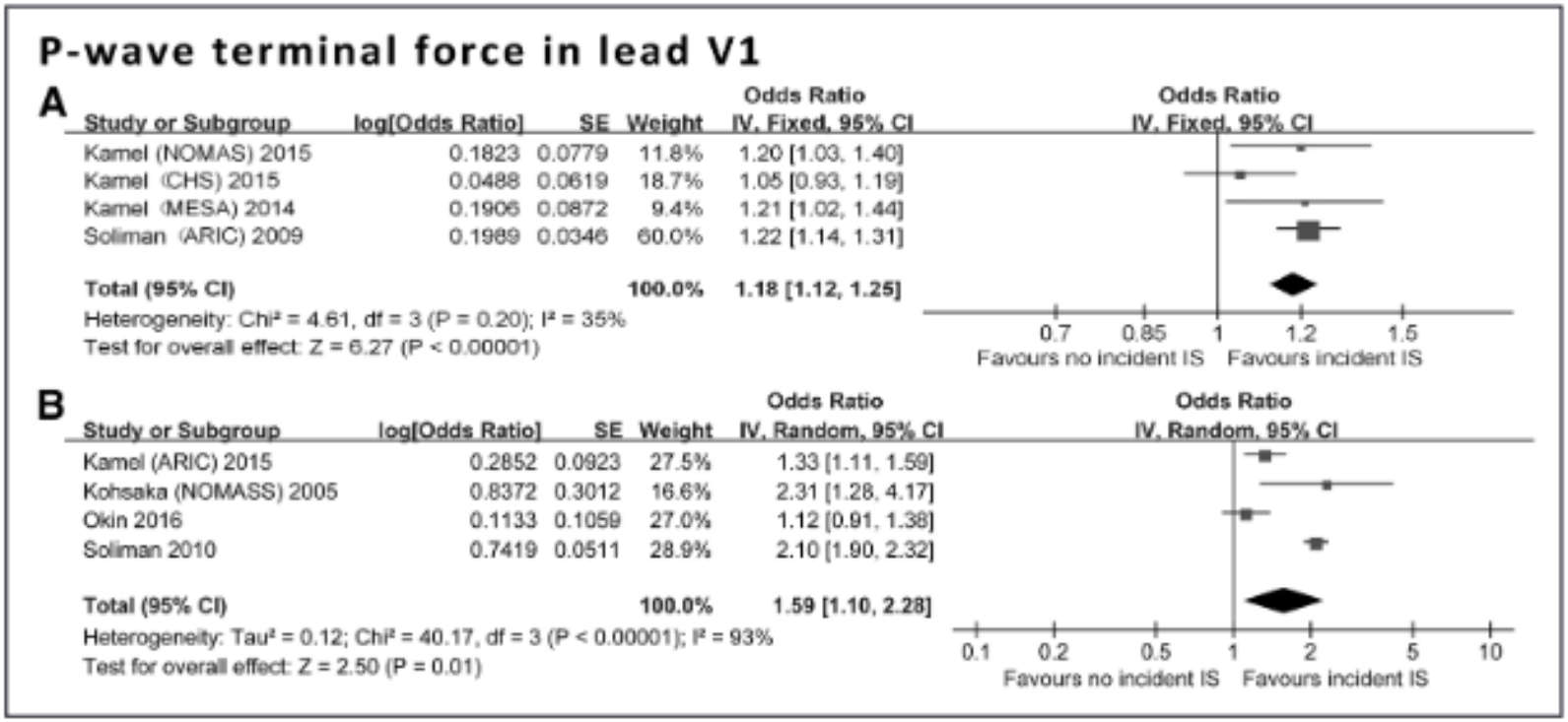
- P wave index; P wave terminal force V1 (X*Y), P wave dispersion, duration





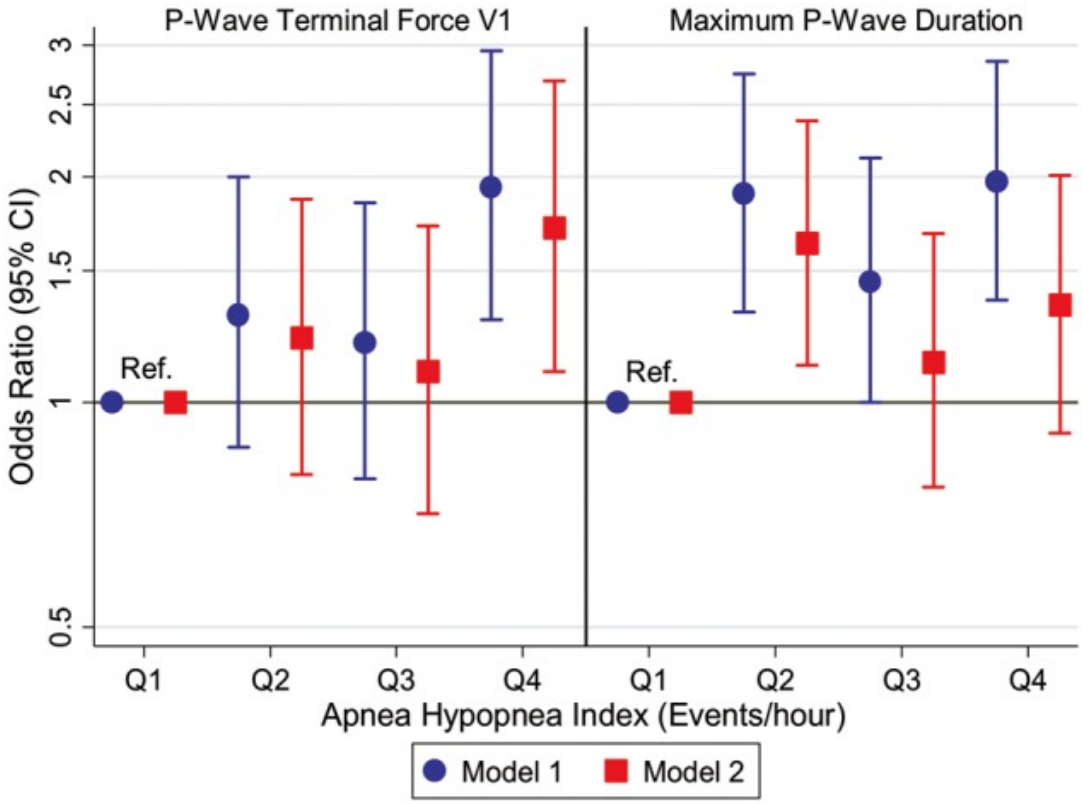
Kwon et al. Sleep Med Review 2018

PTFV1 and stroke risk



He et al. Stroke 2017

OSA-P wave index



MESA Sleep cohort

PTFV1 ≥4000 μV.ms
Maximum p-wave duration ≥120 ms

OSA severity ↑ → Abnormal PTFV1 odds↑

Kwon et al. Europace 2017

P wave index in clinic AF population

OSA measures	$PTFV_1$		$PWAV_1$	
	***β* coefficient**	***p* Value**	***β* coefficient**	***p* Value**
AHI	21.5 [5.4, 37.7]	0.01	2.5 [0.8, 4.2]	0.004
AHI (per 1 *SD*)	611.5 [148.9, 1,079.1]		73.0 [23.0, 122.9]	
Mean O_2 saturation	−171.2 [−317.8, −24.5]	0.02	−10.6 [−26.1, 4.9]	0.18
Mean O_2 saturation (per 1 *SD*)	−539.6 [−971.2, −72.0]		−34.6 [−80.6, 15.4]	

Corotto and Kwon et al Ann Noninvasive Electrocardiology 2019

Summary I

- The prevalence of nocturnal AF is higher in subjects with SA. An association between SA and AF (beyond nocturnal AF) is less well defined.
- A limited number of prospective studies have shown the association between OSA and incident AF. The association appears stronger in the younger individuals.
- Both SA and AF are common in patients with HF but the associations between AF and SA remain unclear in this population.

Summary II

- Coexisting OSA confers greater risk of AF recurrence after catheter ablation than those without OSA and the treatment of OSA with CPAP reduces the risk of AF recurrence after ablation.
- Studies examining the association between sleep duration or quality and AF are scarce.

Future direction

- Obesity, hypertension and metabolic syndrome, while commonly associated with OSA, are potential risk factors for AF, and thus are major confounding factors on the causal pathway between OSA and AF. Study designs strictly controlling for these factors are needed.
- Randomized controlled trials to examine the effect of SA treatment on the incidence or recurrence of AF are needed.

Future direction

- The association between SA and AF has been inconsistent depending on the subtype of SA (i.e., OSA vs. CSA) in the study.
- The most commonly used respiratory measure, AHI, while offering a valuable tool to detect SA, has underappreciated limitations as a metric for quantifying the degree of cardiovascular response to SA. Thus, SA-AF studies based on AHI may have inherent limitations.
- Most investigations have ignored potential effects of other sleep characteristics such as sleep duration that may have implications beyond SA in the pathogenesis of AF. More studies will be needed to clarify the association between other sleep characteristics rather than SA and AF.

Post-test question

Which statement is supported by the strongest evidence?

- A. OSA increases the risk of new onset AF
- B. OSA increases the risk of AF recurrence after catheter-based ablation
- C. Treatment of OSA reduces the recurrence of AF after catheter-based ablation
- D. OSA increases the risk of stroke via increasing AF burden