Sleep Apnea: A Cardiac Problem ?

K. Praveen Vohra, MD, FAASM, FCCP

I have no financial disclosures

K. Praveen Vohra, MD

DISEASE PREVALENCE ADULTS

- Disease Prevalence

Hypertension	29-31 %
Diabetes	4.4-17.9 %
OSA in Men	34%
OSA in Women	17%

IMPACT

Condition	Odds Ratio
Death	3-6 Severe OSA
Incident CHF	1.68
HTN	2-3
Incident Stroke	2.86
Incident Cancer	1.68
Cancer mortality	5x

Cardiovascular Physiology in Sleep

- Heart rate decreases in NREM sleep and further in REM sleep due to increased vagal tone
- COP falls progressively in sleep and nadirs esp. in the last REM cycle early in the morning
- Arterial BP falls in NREM by 5% - 14% and fluctuates in REM sleep

Cardiovascular Physiology in Sleep

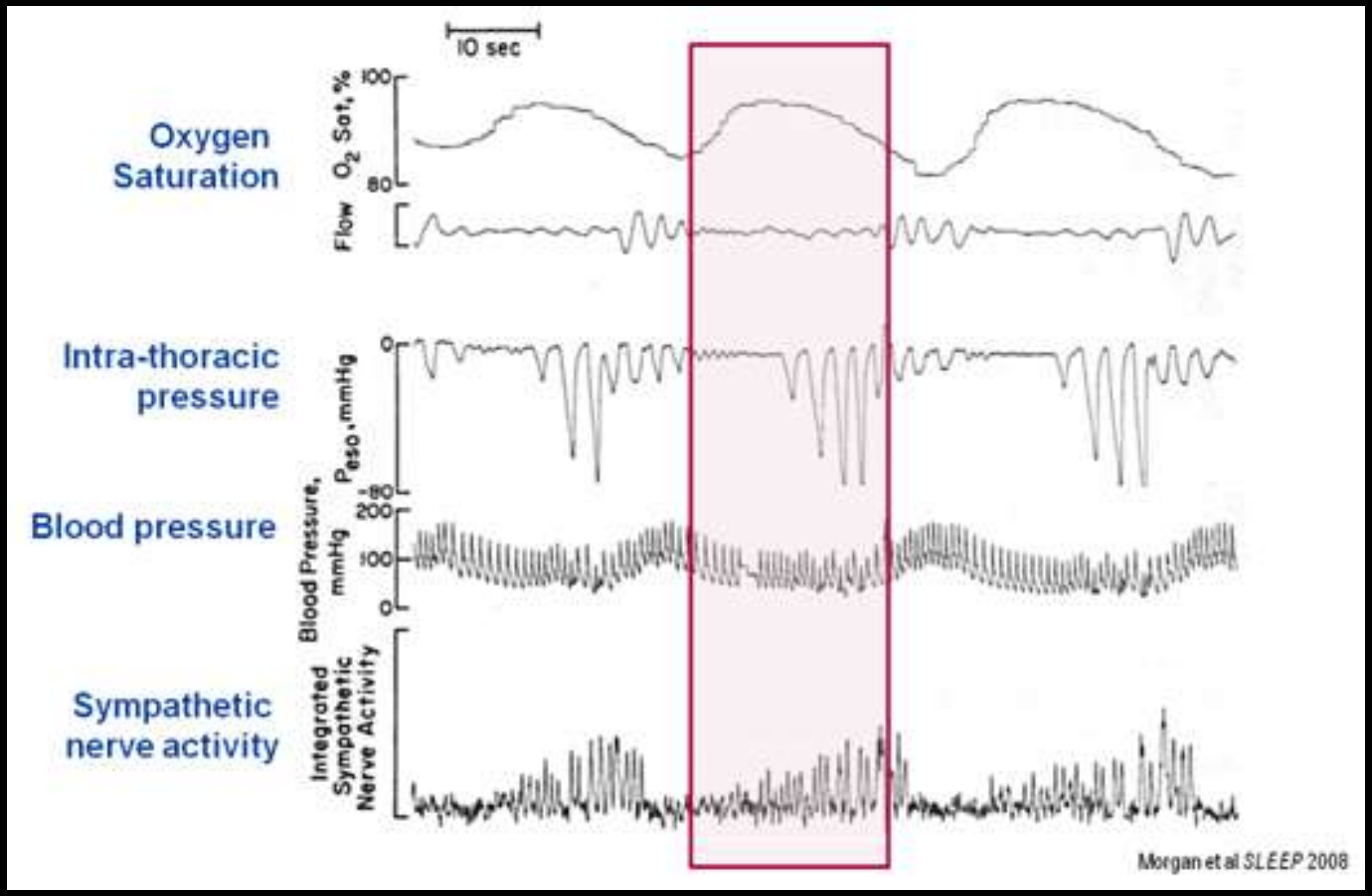
- PA pressure rises slightly in sleep
- SVR decreases in REM sleep
- Blood flow increases in various vascular beds, esp cerebral, in REM sleep

Cardiovascular Physiology in OSA

- Increased
  - Systemic BP by as much as 25%
  - SVR
  - Sympathetic nervous system activity
- Reduced stroke volume and COP
- Increased left ventricular transmural pressure

Cardiovascular Physiology in OSA

- Marked increase in PA pressures esp. in REM sleep
- Increased rate of arrythmias including: sinus arrythmia, sinus bradycardia, heart blocks of all degrees, V Tach
- Decreased cerebral perfusion in apneics even while awake


Oxygen Saturation
Intra-thoracic pressure
Blood pressure
Sympathetic nerve activity
10 sec
100
80
O_2 Sat, %
Flow
0
-80
P_{eso}, mmHg
200
100
0
Blood Pressure, mmHg
Integrated Sympathetic Nerve Activity
Morgan et al SLEEP 2008

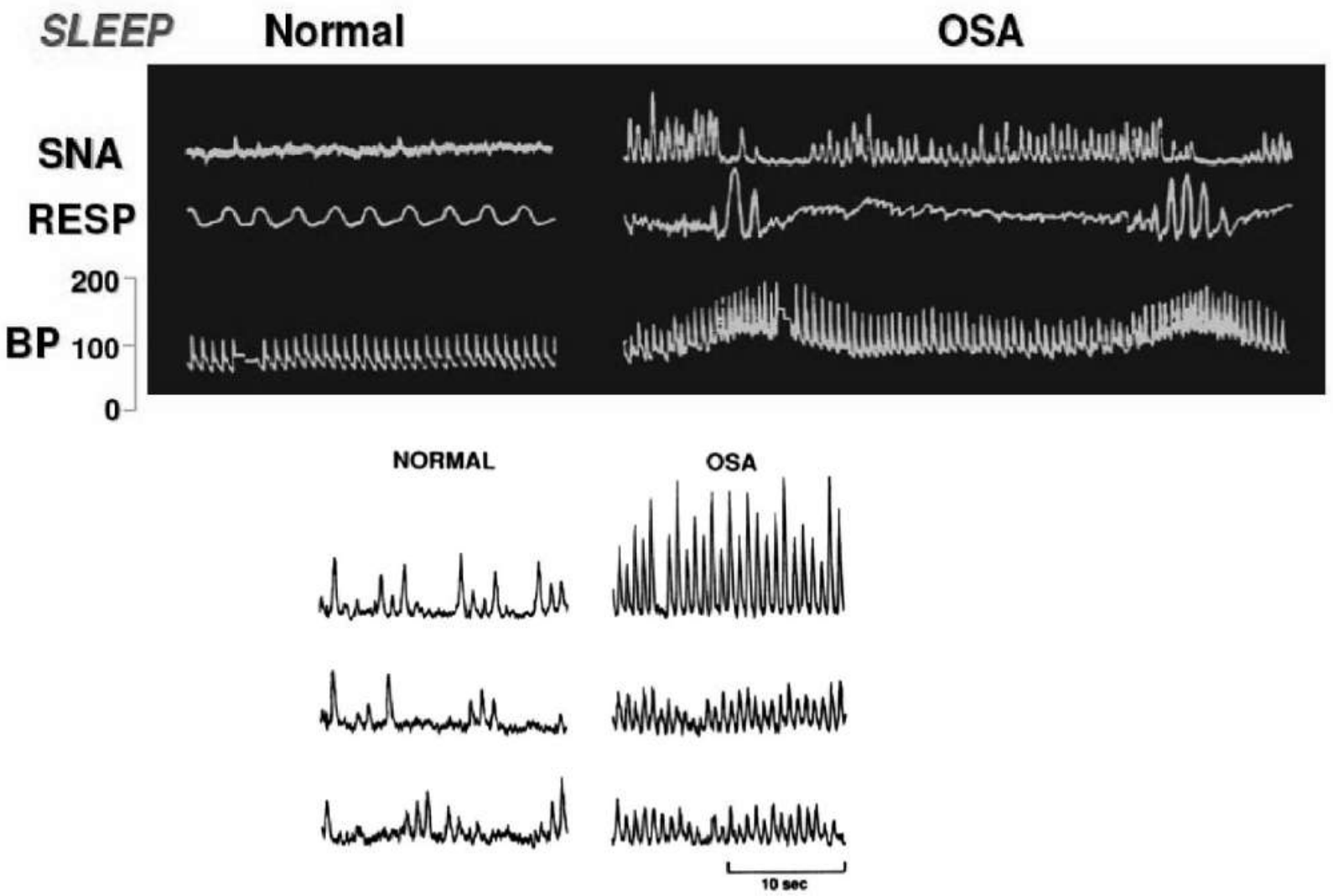
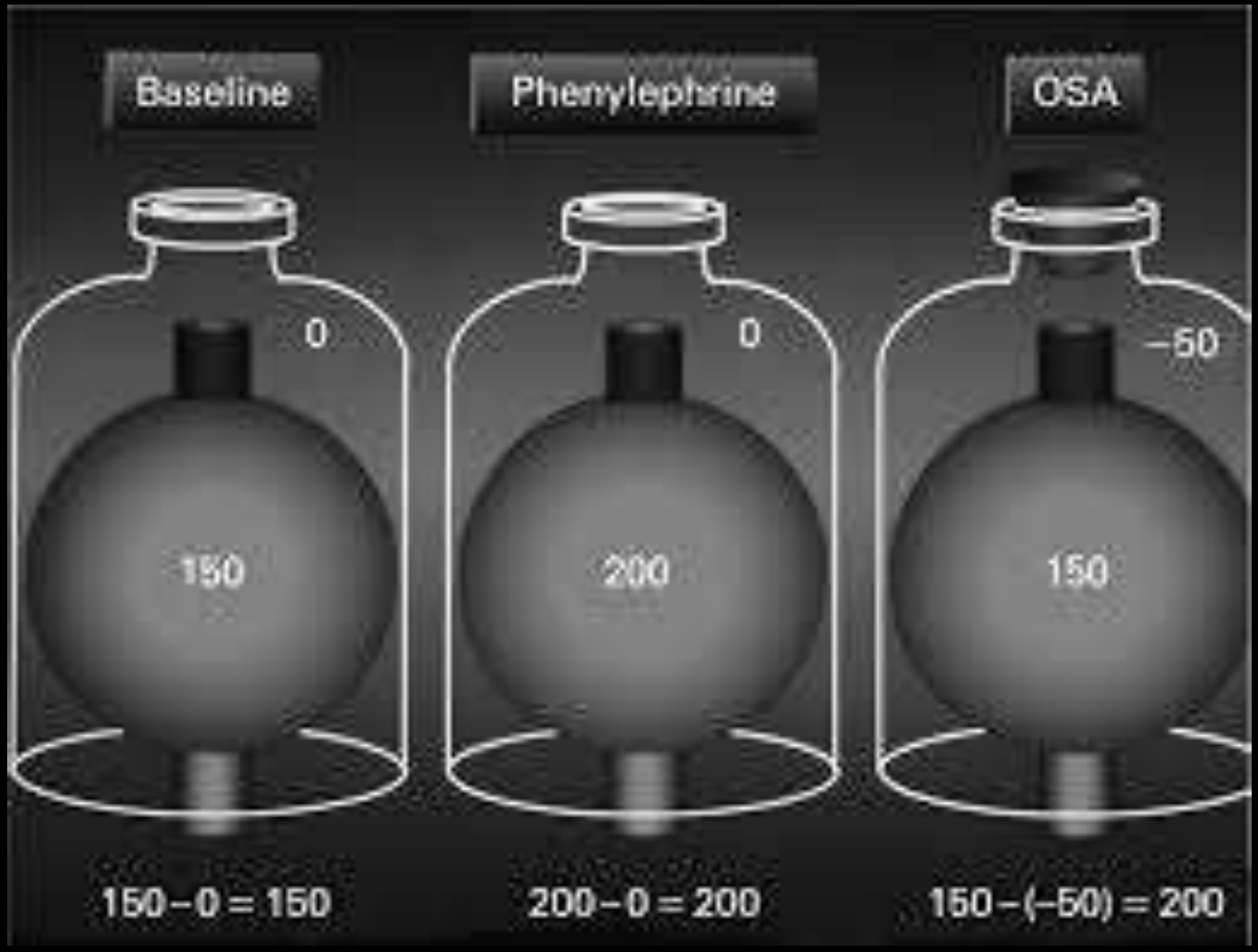
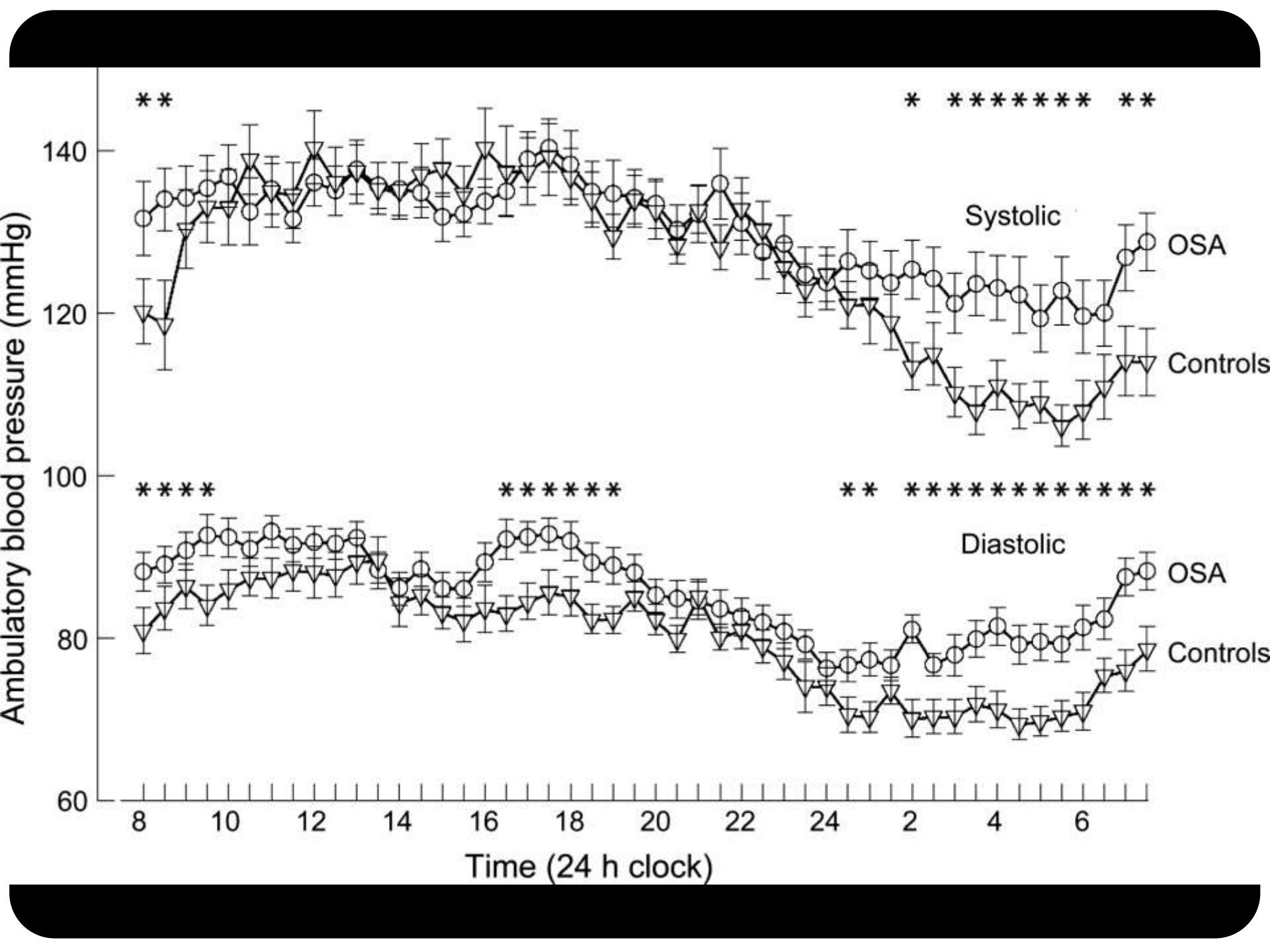


Figure 3—TOP: Peripheral muscle sympathetic neural activity SNA) during sleep in an individual without and with OSA. BOTTOM: Heightened SNA is carried over into normoxic wakefulness. Reproduced with permission reference 2.


Baseline
Phenylephrine
OSA
0
0
−50
150
200
150
150 − 0 = 150
200 − 0 = 200
150 − (−50) = 200


Ambulatory blood pressure (mmHg)
140
120
100
80
60
Systolic
OSA
Controls
Diastolic
OSA
Controls
8
10
12
14
16
18
20
22
24
2
4
6
Time (24 h clock)

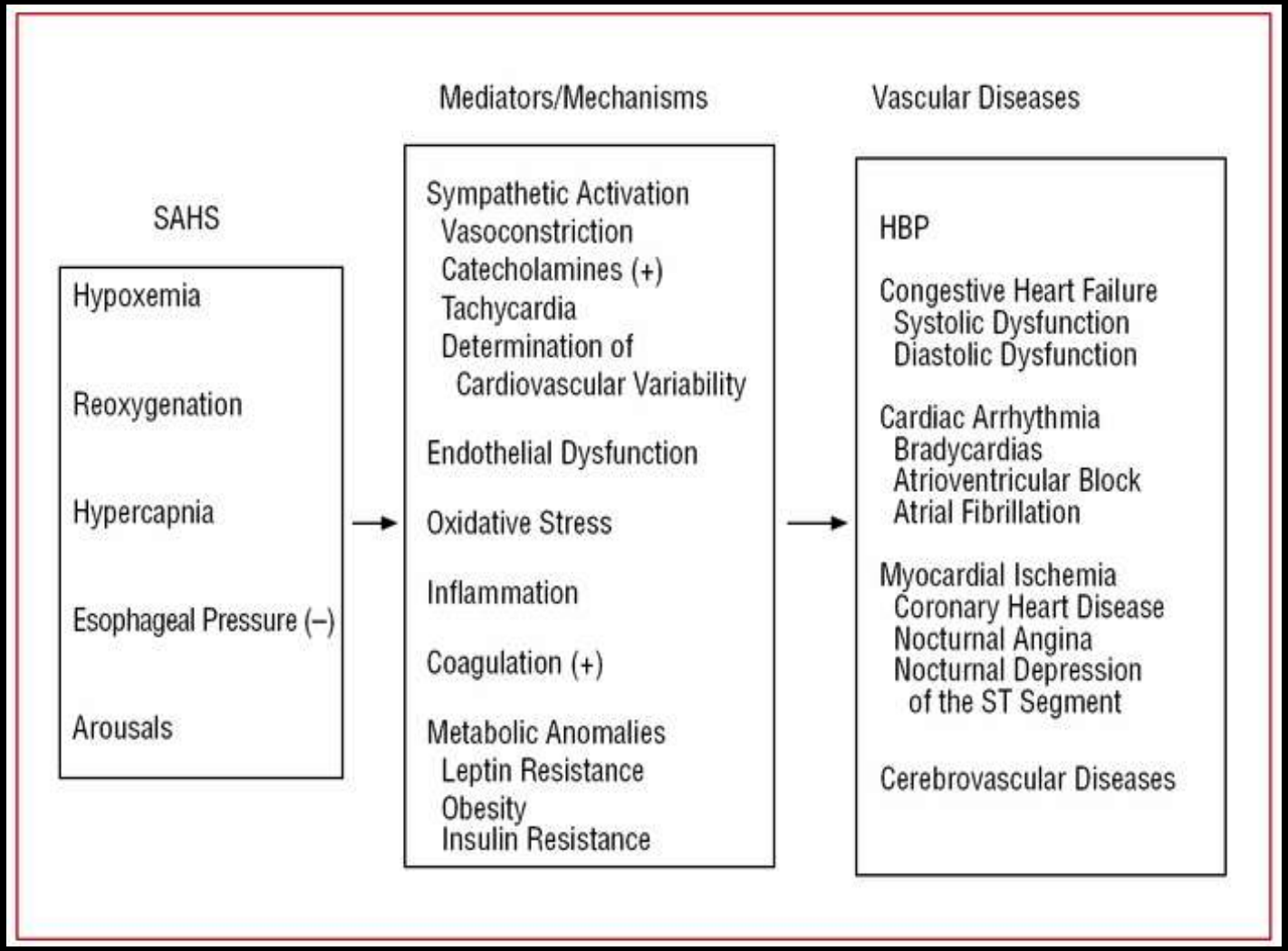
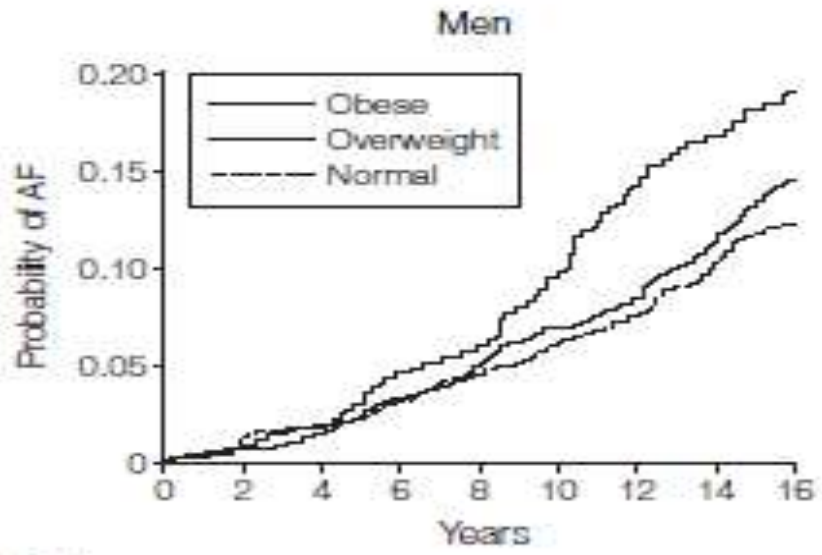

SAHS
Hypoxemia
Reoxygenation
Hypercapnia
Esophageal Pressure (–)
Arousals
Mediators/Mechanisms
Sympathetic Activation
Vasoconstriction
Catecholamines (+)
Tachycardia
Determination of
Cardiovascular Variability
Endothelial Dysfunction
Oxidative Stress
Inflammation
Coagulation (+)
Metabolic Anomalies
Leptin Resistance
Obesity
Insulin Resistance
Vascular Diseases
HBP
Congestive Heart Failure
Systolic Dysfunction
Diastolic Dysfunction
Cardiac Arrhythmia
Bradycardias
Atrioventricular Block
Atrial Fibrillation
Myocardial Ischemia
Coronary Heart Disease
Nocturnal Angina
Nocturnal Depression
of the ST Segment
Cerebrovascular Diseases

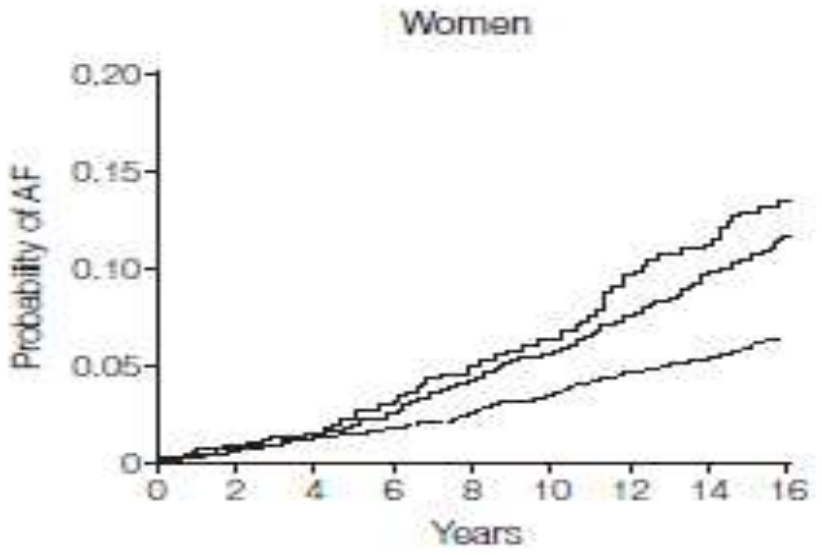
Table 3—The association of untreated sleep disordered breathing with incident coronary heart disease or heart failure events.

AHI Severity Category	Total, n (%)	Incident Events, n (%)	Rate per 1,000 Person Years (95% CI)	Hazard Ratios (95% CI)	
				Adjusted for Age and Sex	Additionally Adjusted for BMI and Smoking
0	238 (21)	17 (7.1)	4.7 (2.8, 7.4)	Reference	Reference
> 0 to ≤ 5	683 (60)	100 (14.6)	10.6 (8.7, 12.9)	1.88 (1.12, 3.16)	1.53 (0.91, 2.59)
5 to ≤ 15	147 (13)	34 (23.1)	18.9 (13.3, 26.1)	2.74 (1.52, 4.96)	1.92 (1.05, 3.53)
15 to ≤ 30	40 (4)	11 (27.5)	21.8 (11.5, 38.0)	2.64 (1.22, 5.72)	1.84 (0.85, 4.02)
≥ 30	23 (2)	10 (43.5)	41.5 (21.1, 73.9)	5.36 (2.41, 11.89)	2.63 (1.13, 6.10)
P trend				< 0.0001	0.017

n = 1,131, excluding 149 participants treated with continuous positive airway pressure at baseline or at follow-up visits. AHI, apnea-hypopnea index; BMI, body mass index; CI, confidence interval.

Figure. Kaplan-Meier Curves Showing Cumulative Hazards of Developing Atrial Fibrillation (AF) in Men and Women, by Baseline Body Mass Index Category





No. at Risk										
Obese	413	380	336	280	238	464	444	397	345	299
Overweight	1216	1143	1023	908	776	898	852	776	696	614
Normal	755	699	614	557	482	1536	1476	1394	1282	1180

Horizontal axis represents time since the baseline examination. Body mass index categories were as follows: normal, <25.0; overweight, 25.0 to <30.0; and obese, ≥30.0.

Table 3. Body Mass Index and Risk of Incident Atrial Fibrillation, Multivariable Models*

Model	Men		Women	
	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
With BMI as a continuous variable (+1 unit)				
Age-adjusted	1.05 (1.02-1.08)	.002	1.04 (1.02-1.07)	.001
Adjusted for clinical variables†	1.04 (1.01-1.07)	.02	1.04 (1.01-1.07)	.01
Adjusted for clinical variables and interim MI/CHF†	1.04 (1.01-1.07)	.02	1.04 (1.01-1.07)	.009
With BMI as a categorical variable				
Age-adjusted				
Normal	1.00		1.00	
Overweight	1.12 (0.85-1.48)	.41	1.20 (0.90-1.62)	.21
Obese	1.69 (1.22-2.35)	.002	1.59 (1.13-2.22)	.008
Trend across categories	1.29 (1.09-1.53)	.003	1.25 (1.06-1.48)	.009
Adjusted for clinical variables†				
Normal	1.00		1.00	
Overweight	1.09 (0.82-1.43)	.56	1.11 (0.83-1.50)	.49
Obese	1.49 (1.06-2.09)	.02	1.45 (1.03-2.05)	.04
Trend across categories	1.22 (1.02-1.44)	.03	1.20 (1.00-1.42)	.046
Adjusted for clinical variables and interim MI/CHF†				
Normal	1.00		1.00	
Overweight	1.10 (0.84-1.46)	.49	1.13 (0.84-1.52)	.42
Obese	1.52 (1.09-2.13)	.02	1.46 (1.03-2.07)	.03
Trend across categories	1.23 (1.03-1.46)	.02	1.20 (1.01-1.43)	.04

Abbreviations: BMI, body mass index; CHF, congestive heart failure; CI, confidence interval; HR, hazard ratio; MI, myocardial infarction.

*Body mass index was calculated as weight in kilograms divided by the square of height in meters. Categories were as follows: normal, <25.0; overweight, 25.0 to <30.0; obese, ≥30.0.

†Clinical variables were age, systolic blood pressure, use of antihypertensive therapy, diabetes mellitus, electrocardiographic left ventricular hypertrophy, prior MI or CHF, regular use of cigarettes in the prior year, and significant heart murmur.

Table 2 Risk of Incident Atrial Fibrillation, Univariate Model

	HR	95% CI	p Value
Age (per 10 yrs)	2.11	1.85–2.41	<0.001
Male gender	1.86	1.22–2.85	0.004
Hypertension	2.85	2.02–4.02	<0.001
Coronary artery disease	5.15	3.56–7.44	<0.001
Heart failure	11.76	7.6–18.20	<0.001
History of smoking	1.82	1.24–2.66	0.002
Diabetes mellitus	2.50	1.66–3.78	<0.001
Body mass index (per 1 kg/m^2)	1.03	1.02–1.05	<0.001
Obstructive sleep apnea (apnea–hypopnea index ≥5)	2.18	1.34–3.54	0.002
Apnea–hypopnea index (per 1 event/h)*	1.31	1.14–1.50	0.0001
Tertiles of apnea–hypopnea index distribution	1.36	1.13–1.64	0.001
Arousal index (per 1 event/h)*	1.65	1.29–2.10	<0.001
Lowest nocturnal oxygen saturation (per −1%)*	3.08	1.72–5.54	<0.001
Mean nocturnal oxygen saturation (per −1%)†	1.30	2.82–4.77	0.05

*For a 1-U change in the logarithm. †For a 0.1-U decrease in the logarithm.
CI = confidence interval; HR = hazard ratio.

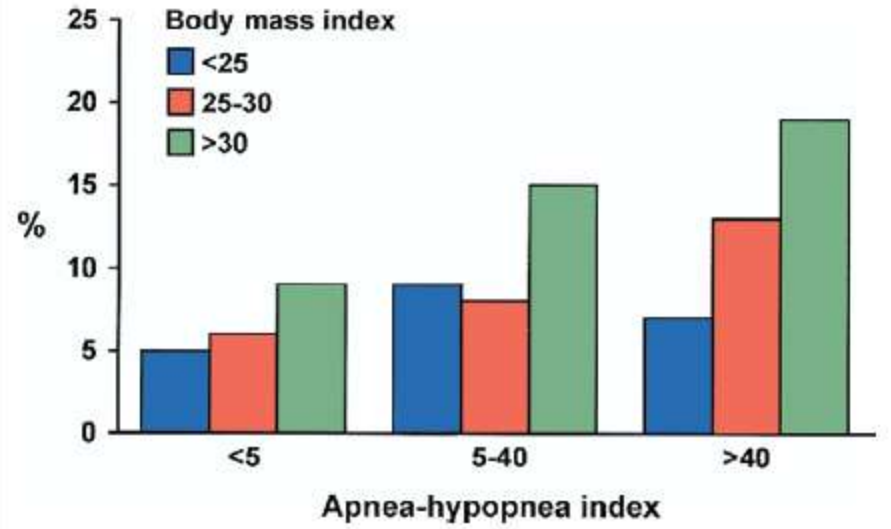


Figure 2 **Incidence of AF Based on the Severity of OSA and Obesity**

Cumulative frequency of incident atrial fibrillation (AF) during an average 4.7 years of follow-up, based on interactions between the body mass index (BMI) and the apnea-hypopnea index (AHI). An AHI <5 represents no obstructive sleep apnea (OSA), an AHI 5 to 40 represents mild to moderate OSA, and an AHI >40 represents severe OSA. A BMI <25 represents normal weight, a BMI 25 to 30 kg/m^2 represents overweight, and a BMI >30 kg/m^2 represents obesity.

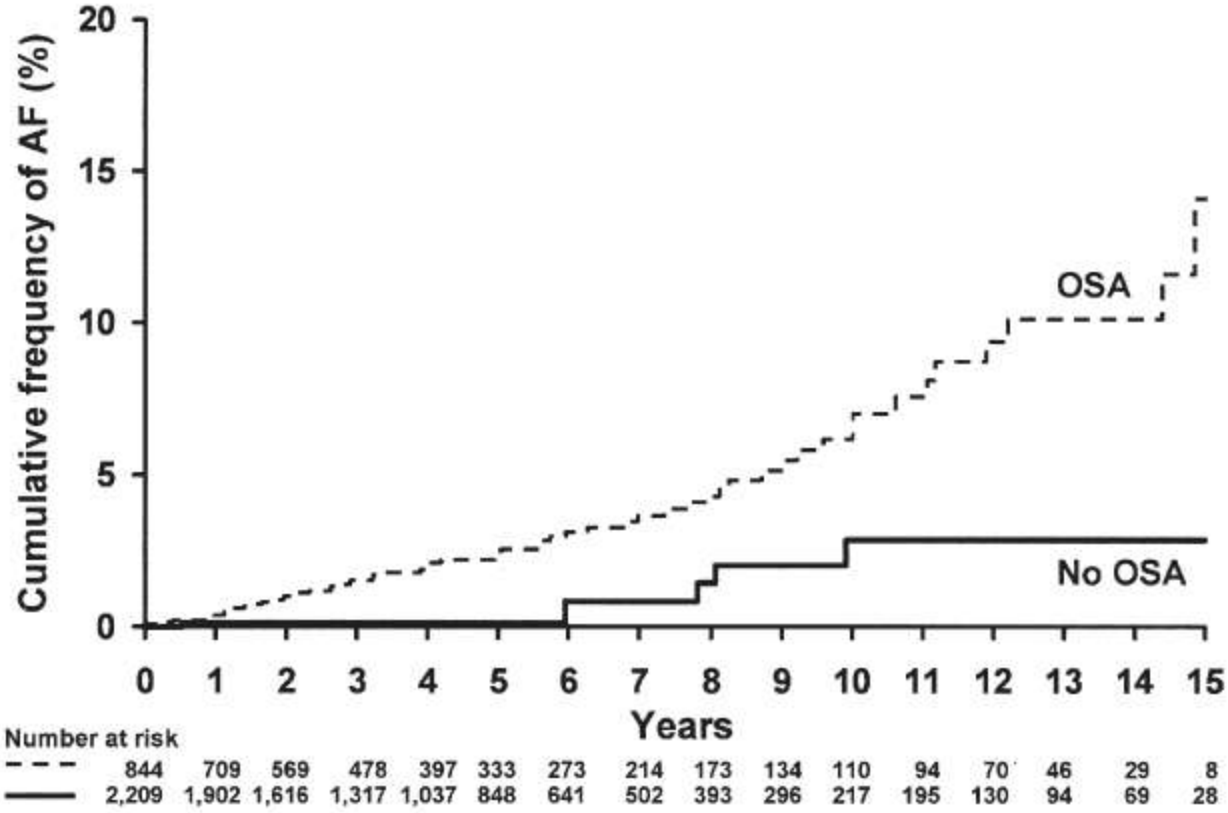
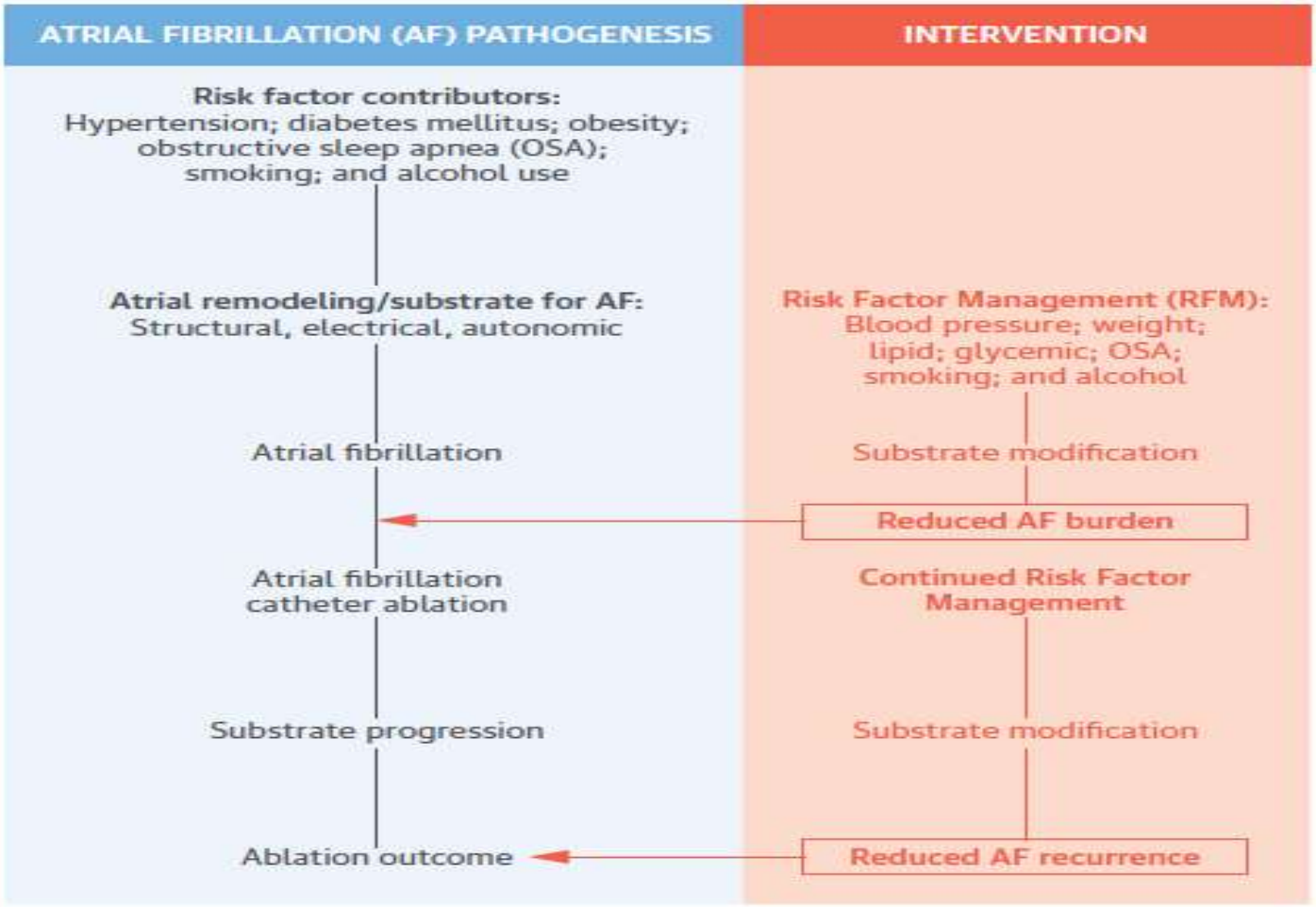


Figure 1 **Incidence of AF Based on Presence or Absence of OSA**

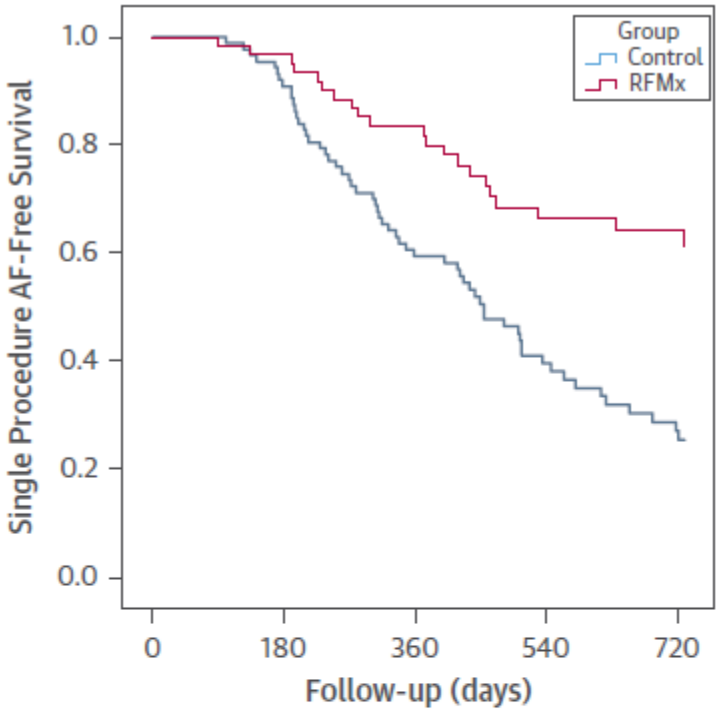
Cumulative frequency curves for incident atrial fibrillation (AF) for subjects <65 years of age with and without obstructive sleep apnea (OSA) during an average 4.7 years of follow-up. $p = 0.002$.

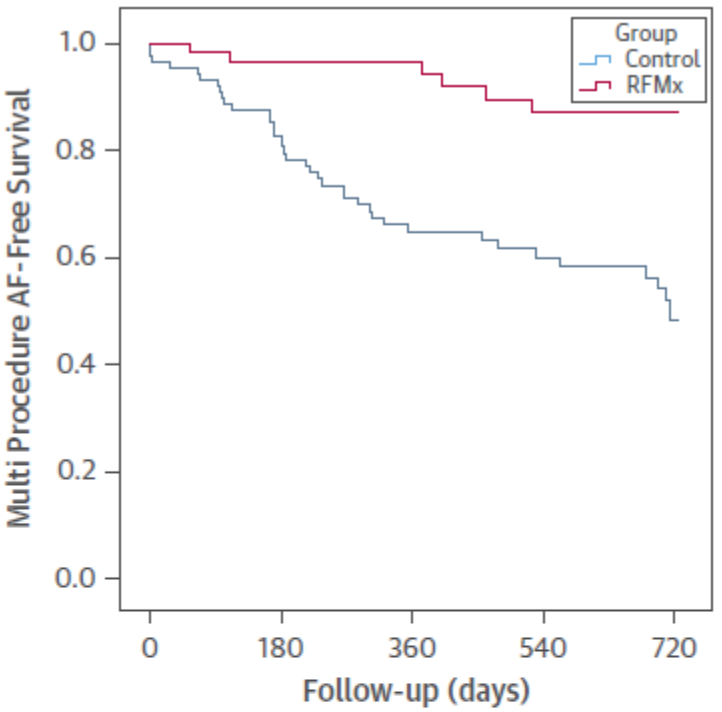


Pathak, R.K. et al. J Am Coll Cardiol. 2014; 64(21):2222–31.

CENTRAL ILLUSTRATION **Impact of Risk Factor and Weight Management on AF Ablation Outcomes**

The schematic demonstrates the natural progression of the atrial fibrillation (AF) substrate and its impact on the maintenance of sinus rhythm **(blue)**. Risk factor management has been demonstrated to reduce the burden of AF and also improve the outcomes of catheter ablation **(salmon)**.





Time (days)	0	180	360	540	730
RFM	61	59	48	33	27
Control	88	79	51	28	16

0	180	360	540	730
61	55	46	32	25
88	72	51	36	23

FIGURE 3 Outcomes of AF Ablation

Kaplan-Meier curves for single-procedure, drug-free, AF-free survival **(left)** and for total AF-free survival (multiple procedures ± drugs) **(right)**. Curves for 2 years are provided, after which <20% of patients completed follow-up. Note that data are provided after the last procedure using a 3-month blanking period. RFM = risk factor management; other abbreviation as in Figure 1.

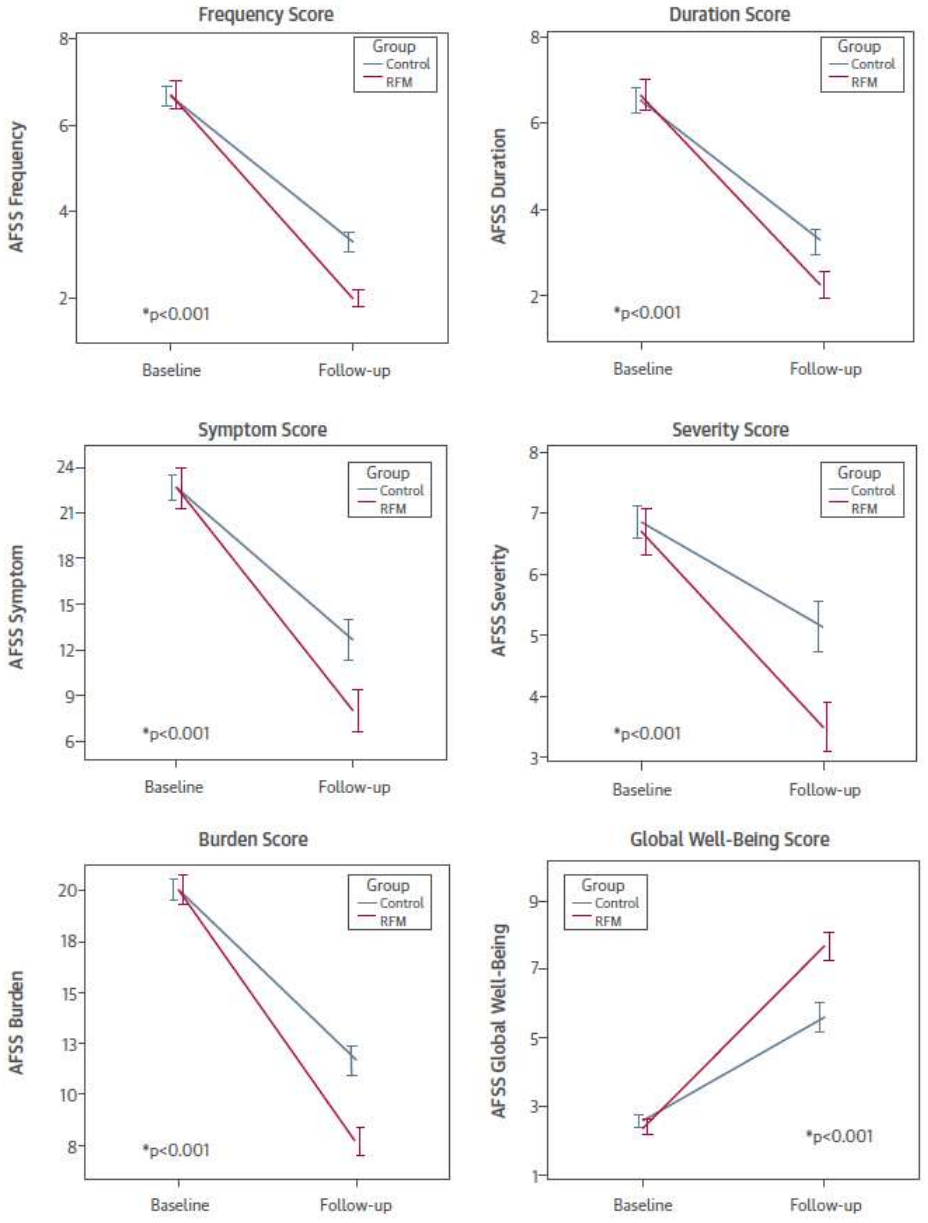


FIGURE 2 Burden of AF

Changes in AF burden according to scores on the Atrial Fibrillation Severity Scale (AFSS) questionnaire at baseline and at final follow-up. **Error bars** indicate 95% confidence intervals. RFM = risk factor management; other abbreviation as in Figure 1.

Sleep Apnea: A Cardiac Problem ?

You Bet !!

References

- Peppard PE, Young T, Barnet JH, Palta M, Hagen EW, Hla KM, authors. Increased prevalence of sleep-disordered breathing in adults. Am J Epidemiol. 2013;177:1006–1014 . (Slide 3)

- Somers VK, Dyken ME, Clary MP, Abboud FM. Sympathetic neural mechanisms in obstructive sleep apnea. J Clin Invest 1995;96:1897-904. (Slide 10)

- Should Sleep Apnoea be a specific target of therapy in chronic heart failure? J S Floras, Heart 2009; 95: 1041-1046. (Slide 11)

- Coronary Heart Disease Incidence in Sleep Disordered Breathing: The Wisconsin **Sleep Cohort Study** Khin Mae Hla, MD, MHS[1]; Terry Young, PhD[2]; Erika W. Hagen, PhD[2]; James H. Stein, MD[1]; Laurel A. Finn, MS[2]; F. Javier Nieto, MD, PhD[2]; Paul E. Peppard, PhD. Sleep vol 38 (5), 2015 (Slide 14)

References

- Obesity and the Risk of New-Onset Atrial Fibrillation. Thomas J. Wang, MD, Helen Parise, ScD, Daniel Levy, MD, Ralph B. D'Agostino, Sr, PhD, Philip A. Wolf, MD, Ramachandran S. Vasan, MD, Emelia J. Benjamin, MD, ScM . JAMA vol. 292, no.20, 2004 (Slides 15-16)

- Obstructive Sleep Apnea, Obesity, and the Risk of Incident Atrial Fibrillation. Apoor S. Gami, MD,*† Dave O. Hodge, MS,‡ Regina M. Herges, BS,‡ Eric J. Olson, MD,†§, Jiri Nykodym, BS,*† Tomas Kara, MD,*† Virend K. Somers, MD, PHD, FACC*†. JACC vol 49, No.5, 2007 (Slides 17-19)

- Aggressive Risk Factor Reduction Study for Atrial Fibrillation and Implications for the Outcome of Ablation The ARREST-AF Cohort StudyRajeev K. Pathak, MBBS,* Melissa E. Middeldorp,* Dennis H. Lau, MBBS, PHD,* Abhinav B. Mehta, MACTST,y Rajiv Mahajan, MD,* Darragh Twomey, MBBS,* Muayad Alasady, MBBS,*y Lorraine Hanley, BSC,*Nicholas A. Antic, MBBS, PHD,z R. Doug McEvoy, MBBS, MD,z Jonathan M. Kalman, MBBS, PHD,xWalter P. Abhayaratna, MBBS, PHD,k Prashanthan Sanders, MBBS, PHD* . JACC, vol 64, no.21, 2014 (Slides 20-22)