CMHC
Cardiometabolic Health Congress

www.cardiometabolichealth.org

Foundations of Cardiometabolic Health Certification Course

Certified Cardiometabolic Health Professional (CCHP)

Cardiology and Sleep Apnea - The Intersection and Collision: A Deeper Dive

Lee A. Surkin, MD, FACC, FCCP, FASNC, FAASM
Founder, American Academy of Cardiovascular Sleep Medicine
President, Empire Sleep Medicine

Outline

- Clinical Vignette
- Demographics
- Cardiovascular Effects of SDB
- Hypertension
- Arrhythmias
- Congestive Heart Failure
- Coronary Artery Disease
- Cerebrovascular Accident
- Treatment Options

CMHC
Cardiometabolic Health Congress

www.cardiometabolichealth.org

Foundations of Cardiometabolic Health Certification Course

Certified Cardiometabolic Health Professional (CCHP)

Obstructive Sleep Apnea: Demographics & Cardiovascular Effects

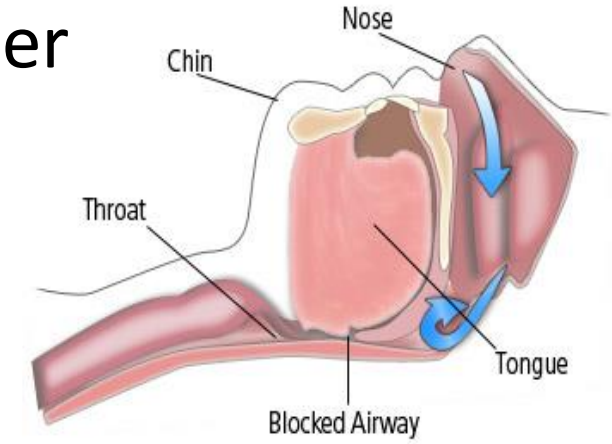
Lee A. Surkin, MD, FACC, FCCP, FASNC, FAASM
Founder, American Academy of Cardiovascular Sleep Medicine
President, Empire Sleep Medicine

Clinical Vignette

- NM: 57 yo male, BMI 42, HTN, Hypercholesterolemia, Type 2 DM, Tobacco abuse
- Sedentary with Excessive daytime sleepiness
- Shake the walls snoring. Spouse sleeps in separate room
- BP meds (ACE-inhibitor and beta blocker), statin, aspirin, Oral DM agent, Omega 3

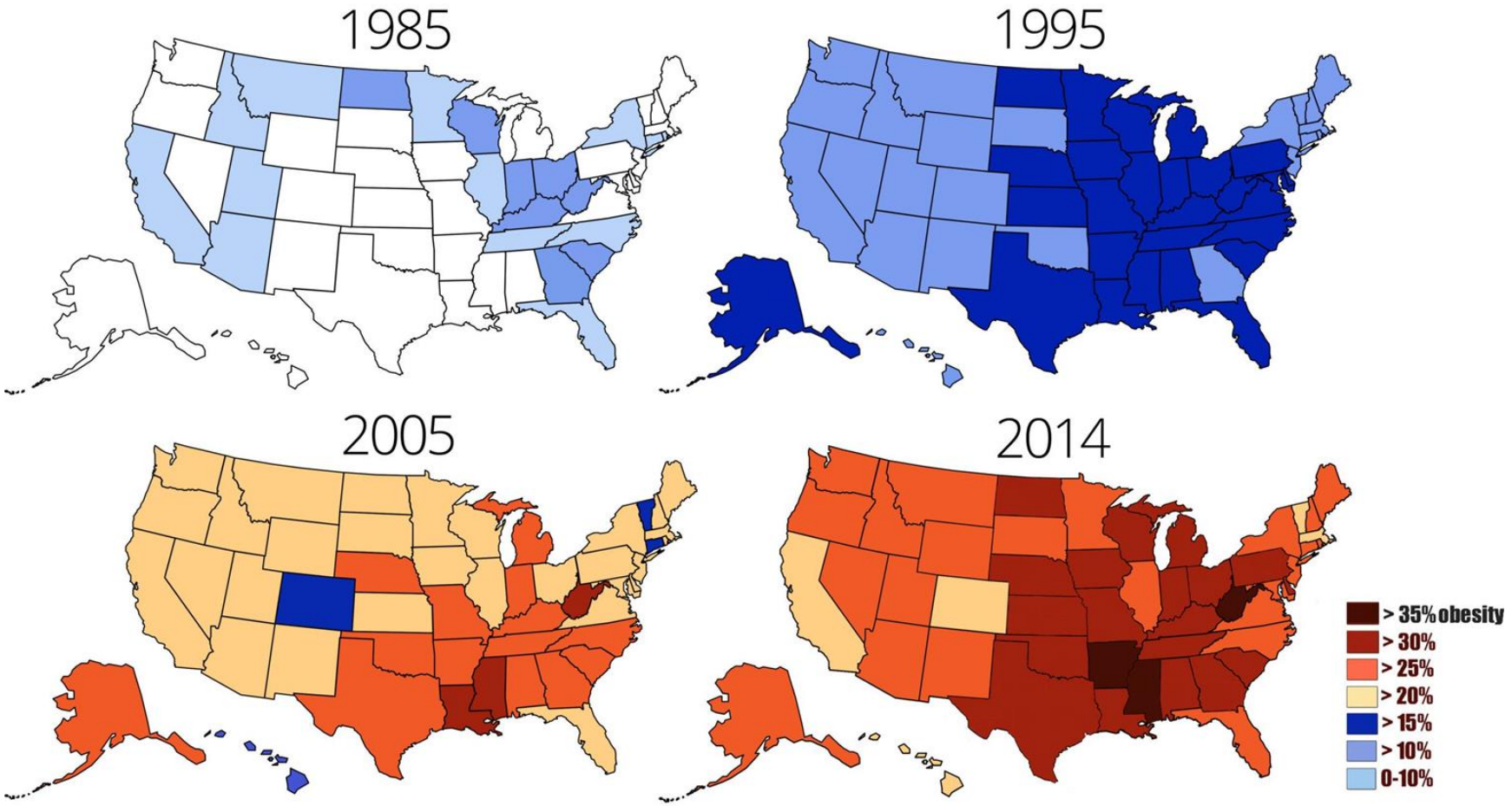
Demographics of Obstructive Sleep Apnea

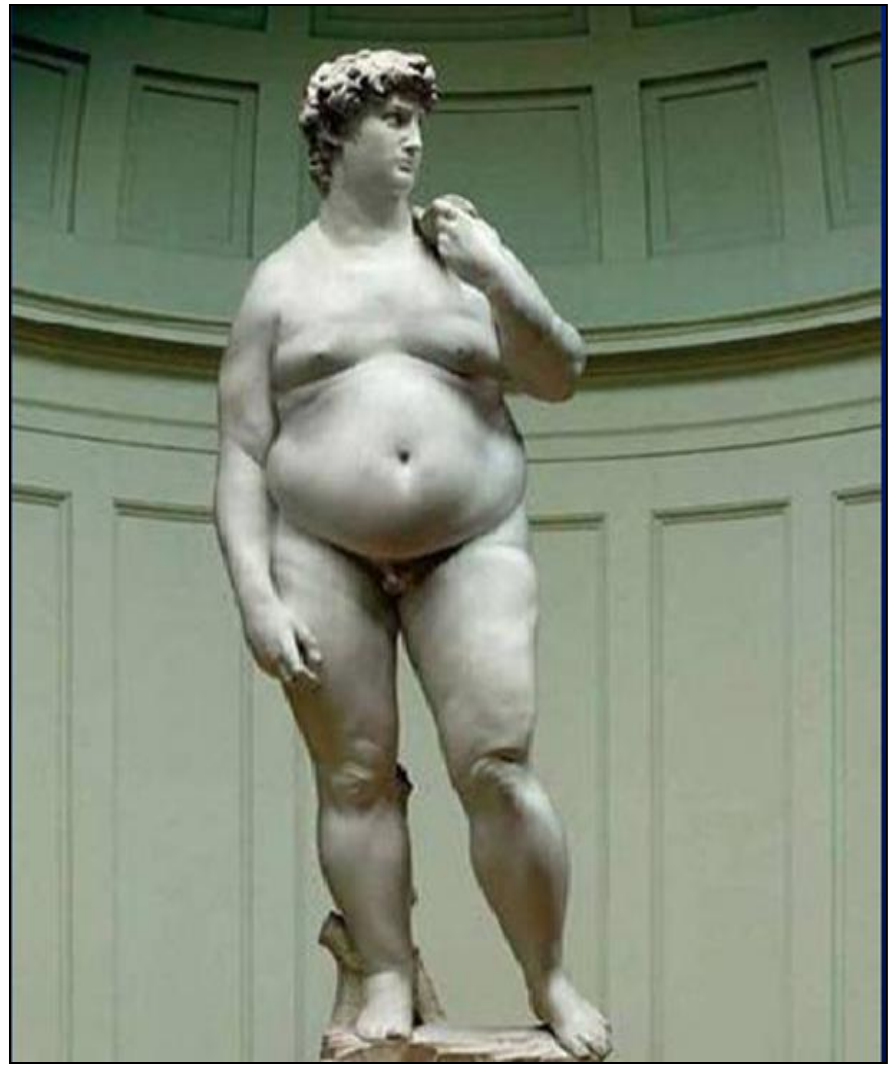
- 4% of men and 2% of women-
  - when symptoms and syndrome present
- 24% of men and 9% of women-
  - based on abnormal sleep study alone
- 20-40 million Americans with OSA- 80-85% undiagnosed
- Incidence of OSA increases with Age
- Incidence of Cardiovascular disease increases with Age
- OSA and CV risk factors tend to cluster together



Obesity:

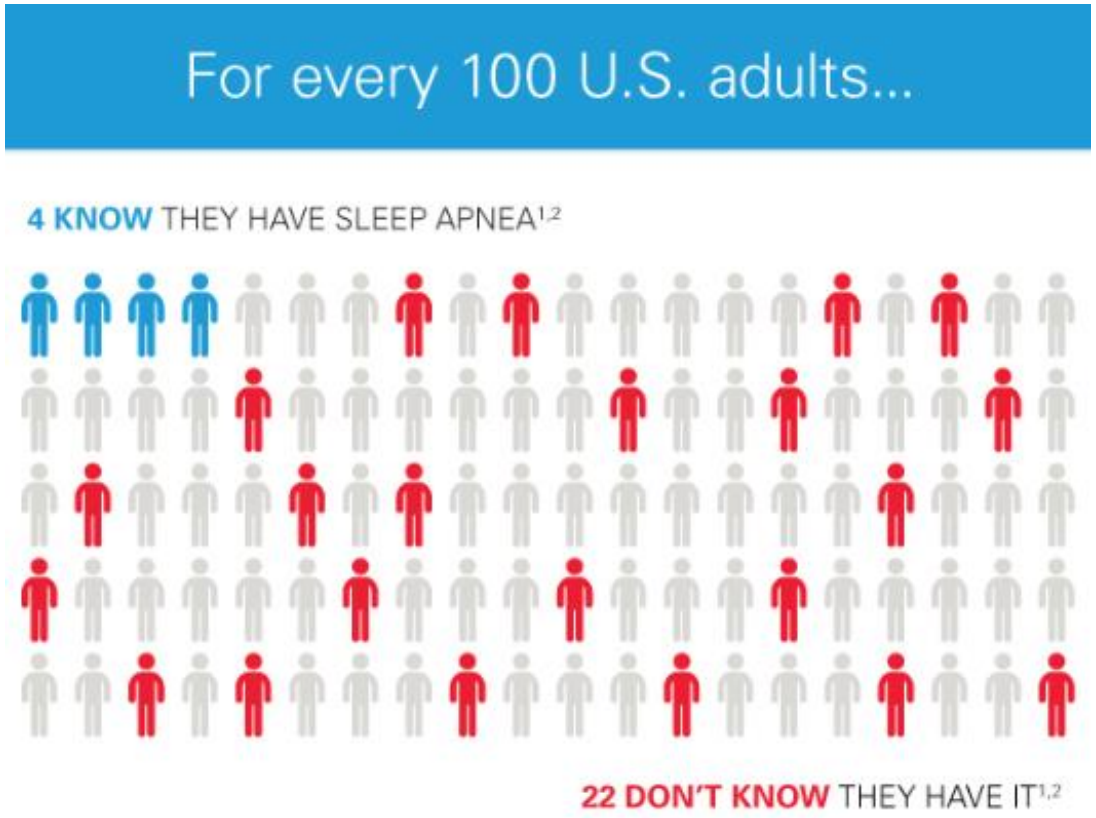
The single biggest risk factor for OSA explosion?

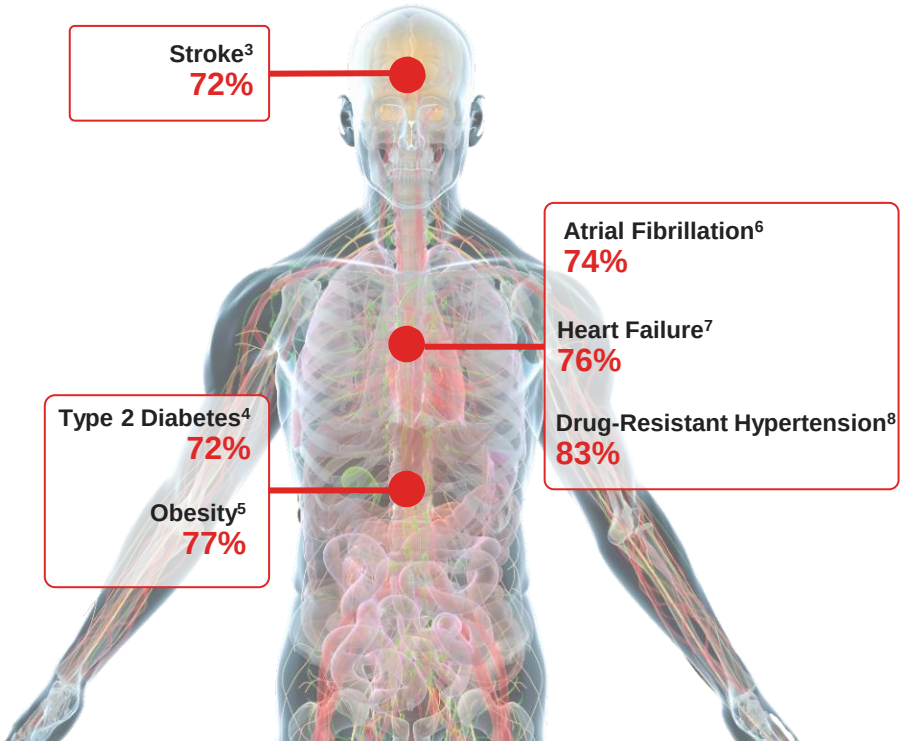




Sleep apnea is more than 80% undiagnosed…

….and is highly prevalent in other chronic conditions





1 Peppard PE et al. *Am J Epidemiol* 2013
2 Young T et al. *Sleep* 1997

3 Johnson KG and Johnson DC. J Clin Sleep Med 2010
4 Einhorn D et al. Endocr Pract 2007
5 O'Keeffe T and Patterson EJ. Obes Surg 2004

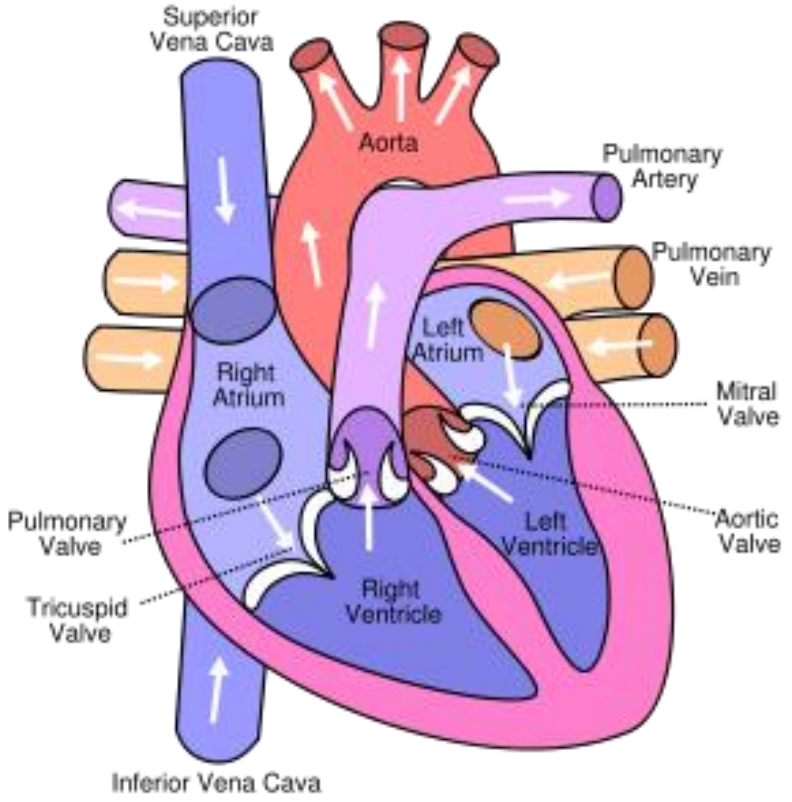
6 Bitter T et al. Dtsch Arztebl Int. 2009
7 Oldenburg O et al. Eur J Heart Fail 2007
8 Logan AG et al. J Hypertens 2001

Cardiovascular Disease

- #1 killer since 1990
- In 1999, 33% of deaths from CVD occurred in patients over 75 years old
- Need new Paradigms and Treatments
- Death from Myocardial Infarction typically occurs 6am-Noon.
- Death from OSA occurs Midnight - 6am

Independent Predictors of Myocardial Infarction

Risk Factor	Odds Ratio
Standard	1.0
Overweight	7.1
Hypertension	7.8
Smoking	11.1
OSA (>5.3)	23.3



Hung, et.al http://www.ncbi.nim.nih.gov/pubmed/1973968

Normal Sleep Physiology
NREM 75-80%

- Decreased sympathetic nerve activity
- “Nocturnal Dipping” 10-15% decrease in bp following a circadian rhythm pattern
- Decreased cerebral blood flow
- Regular breathing pattern
- Decreased minute ventilation
- Decreased muscle tone

Somers: NEJM 2003. Chokroverty: Sleep Disorders Medicine 1999

Normal Sleep Physiology
REM 20-25%

- Sympathetic nerve activity, HR and BP similar to wake
- Increased cerebral blood flow
- Irregular breathing pattern
- Respiration dependent on diaphragm
- Absent muscle tone

Somers: NEJM 2003.
Chokroverty: Sleep Disorders Medicine 1999

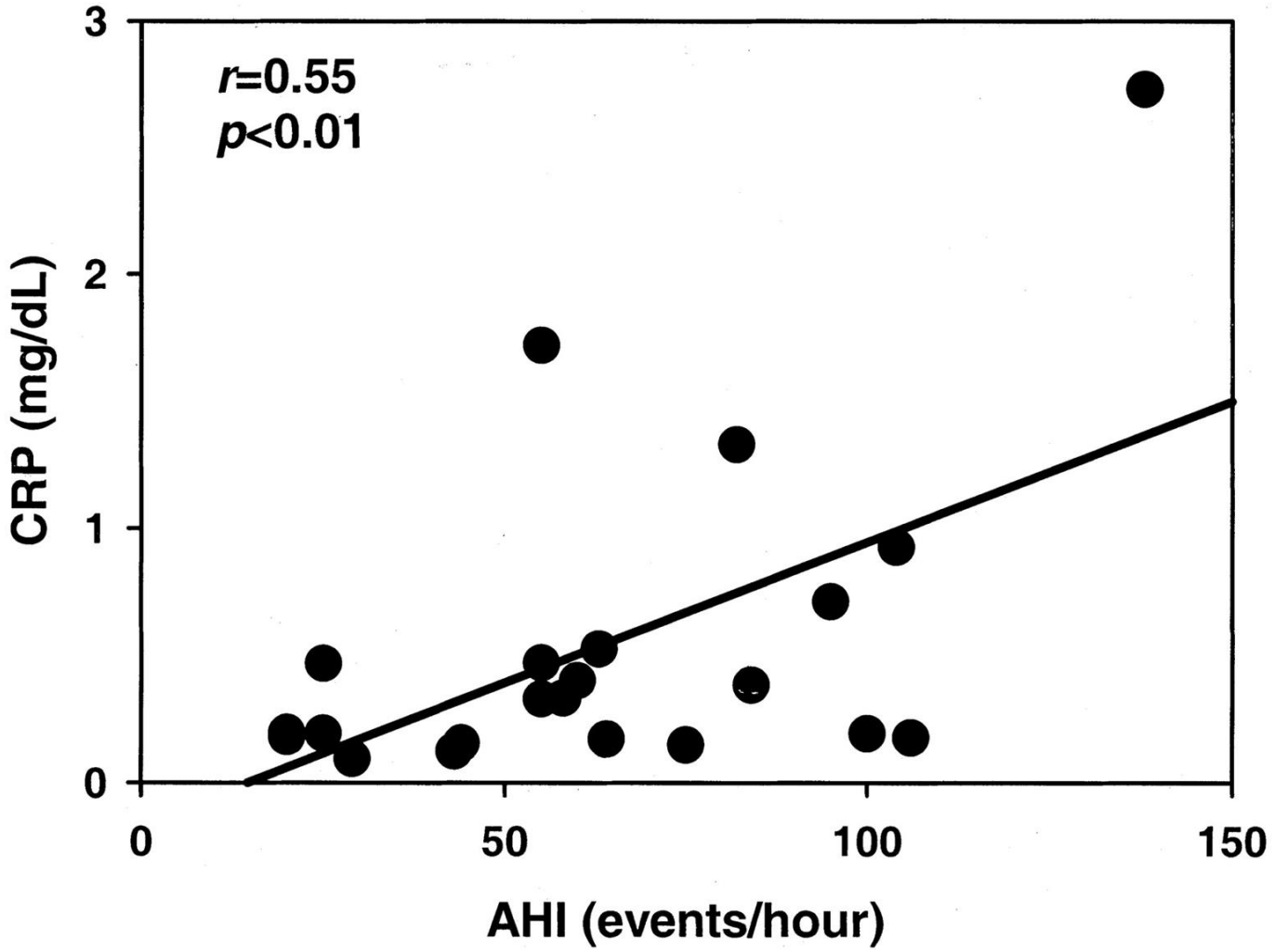
Cardiovascular Effects of Apnea

- Apnea: a cessation of breathing for a minimum of 10 seconds
- Tends to result in decreased blood O_2 and increased CO_2
- Hypoxia independently association with CVD
- Nervous system responds by increasing heart rate and blood pressure and constricting blood vessels in periphery
- Mueller Maneuver
  - Airway closure, increased negative intra-thoracic pressure resulting in increase cardiac pressures
- Alteration of heart rate and blood pressure variability

Transmyocardial Pressure

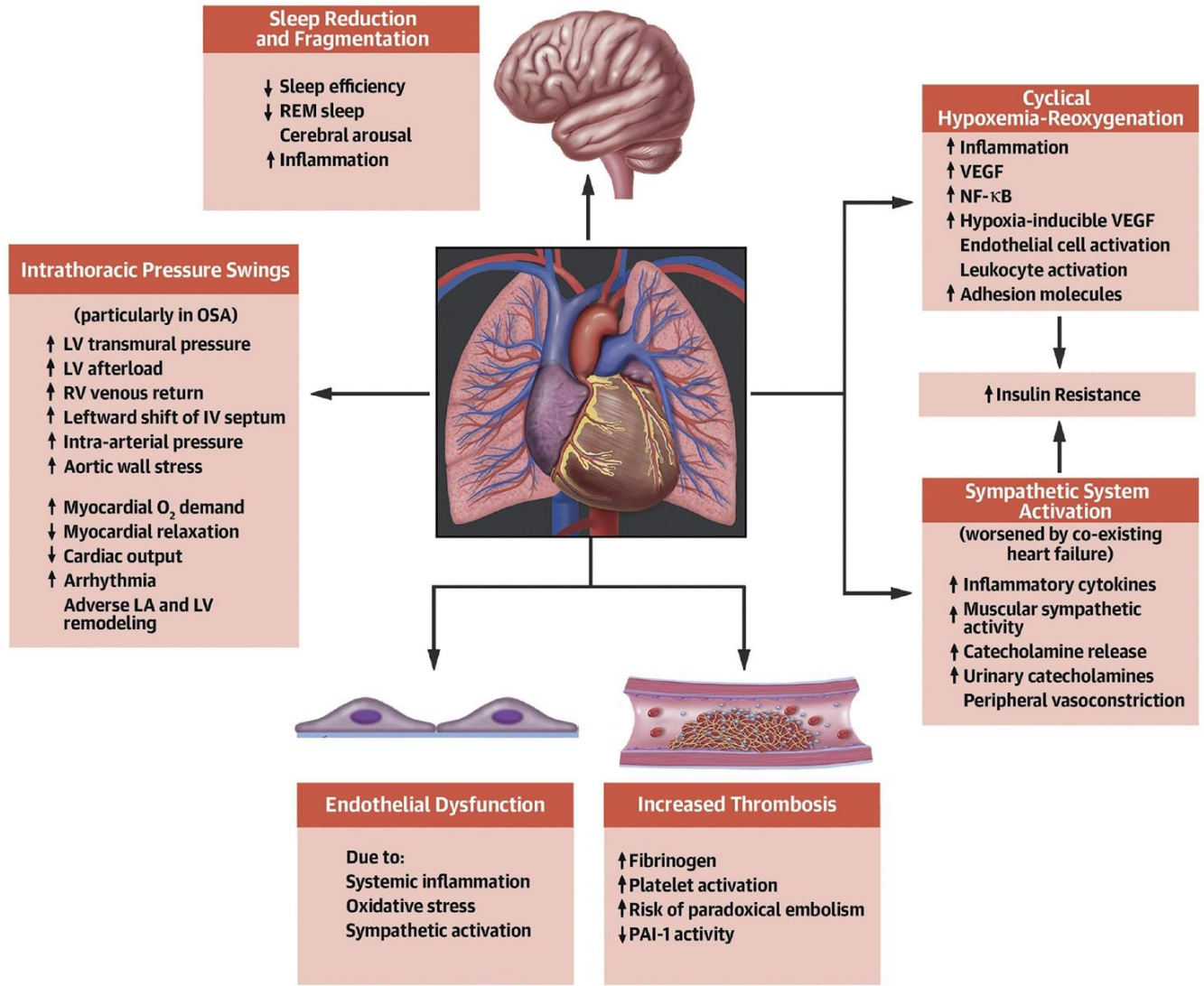
- Decrease in pleural pressure with inspiration and increases with positive airway pressure
- Transmural pressure of heart = intracardiac pressure minus extracardiac pressure (pericardial or pleural)
- Transmyocardial pressure determines wall stress/afterload
- Each inspiration increases transmyocardial pressure
- PAP decreases preload and afterload

OSA: An Inflammatory Disease



Shamsuzzaman, A. S.M. et al. Circulation 2002;105:2462-2464

CENTRAL ILLUSTRATION: Pathophysiological Abnormalities in Sleep Disordered Breathing



Cowie, M.R. et al. J Am Coll Cardiol. 2021;78(6):608-624.

Cardiovascular Manifestations of OSA

- Vascular inflammation
- Clotting tendency
- Oxidative stress
- Hypertension, Pulmonary Hypertension
- Diastolic Dysfunction
- Endothelial dysfunction
- Obesity
- Arrhythmias
- CHF
- Diabetes Mellitus / Metabolic syndrome

****Comparing variables leading to CV death- OSA carries greater risk than Diabetes, Hypertension and Smoking****

CMHC
Cardiometabolic Health Congress

www.cardiometabolichealth.org

Foundations of Cardiometabolic Health Certification Course

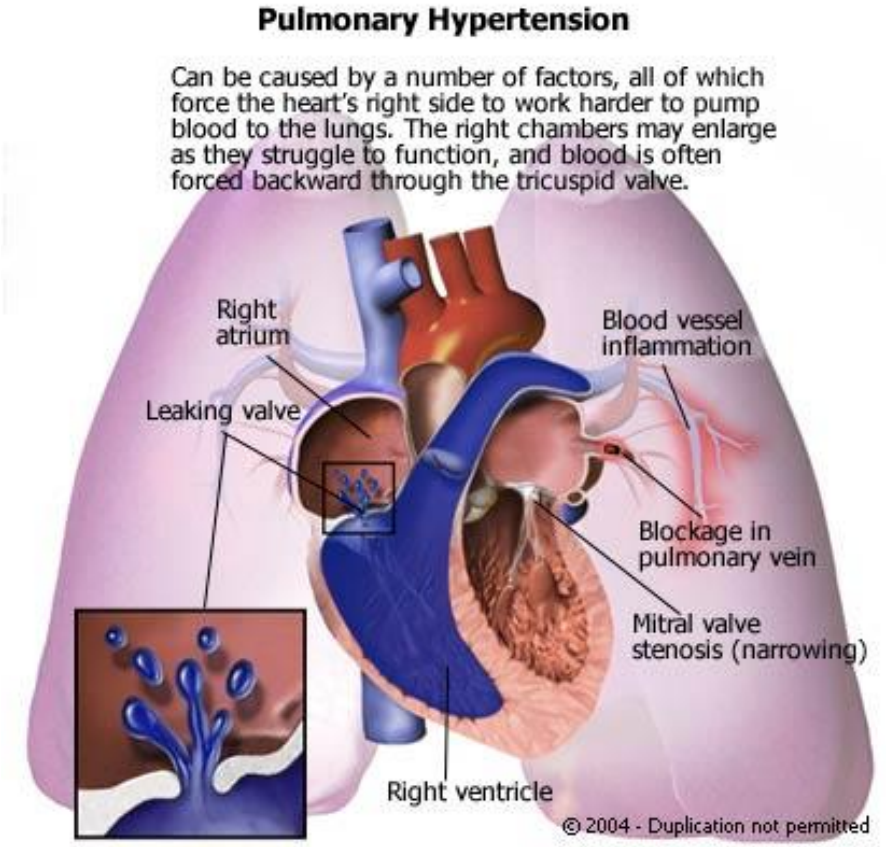
Certified Cardiometabolic Health Professional (CCHP)

OSA & Hypertension

Lee A. Surkin, MD, FACC, FCCP, FASN, FAASM
Founder, American Academy of Cardiovascular Sleep Medicine
President, Empire Sleep Medicine

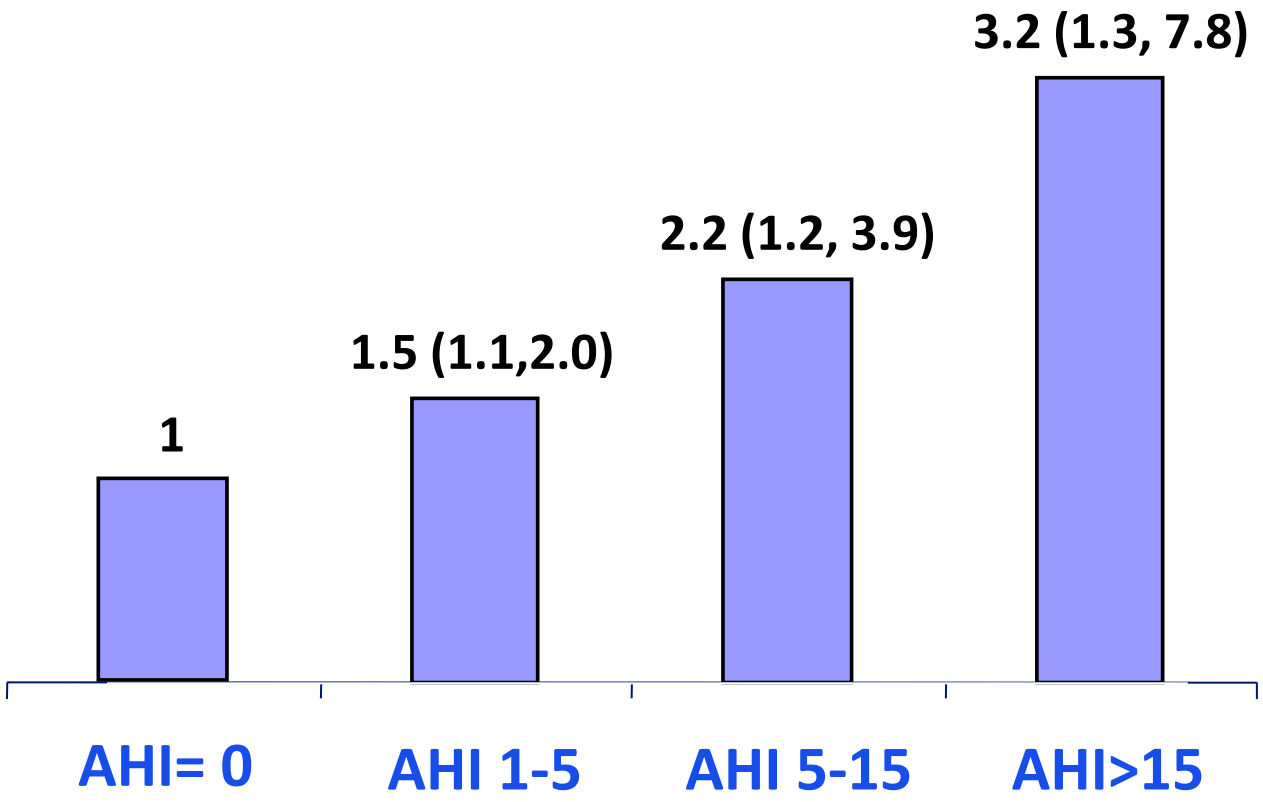
Hypertension

- 50% of OSA patients have hypertension
- 30% of hypertensive patients have OSA
- More difficult to control as OSA worsens
- OSA present in 65-80% of patients with drug-resistant HTN
- JNC 7 concluded that OSA is an independent cause of hypertension
- Treating OSA improves hypertension



Silverberg DS, et al Curr Opin Nephrol Hypertens 1998;7:4:353-357
Johnson DA, et al Circulation 2019;139:1275-1284

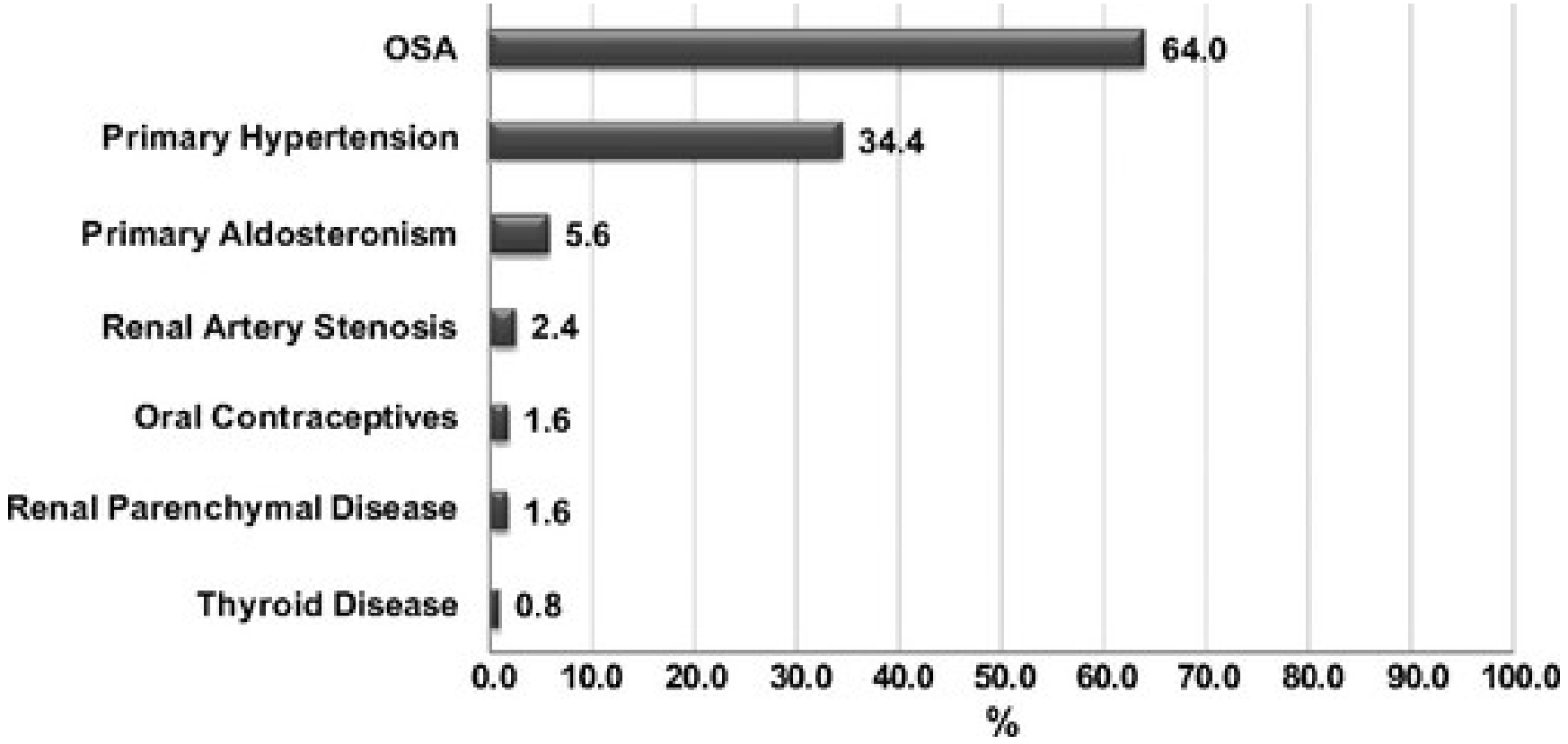
Odds Ratios for Incident Hypertension at 4-year F/U With Baseline Ahi>0 Wisconsin Sleep Cohort Study



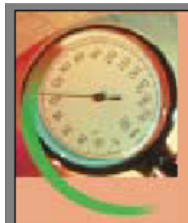
*adjusted for baseline Hypertension, Age, Gender, BMI, Waist Circumference, Alcohol, and Tobacco Use

PEPPARD ET AL, NEJM 2000

Prevalence of Secondary Causes Associated With Resistant Hypertension



Pedrosa R et al. Hypertension 2011:58:811-817



Reference Card From the

Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7)

EVALUATION

Classification of Blood Pressure (BP)*

Category	SBP mmHg		DBP mmHg
Normal	<120	and	<80
Prehypertension	120–139	or	80–89
Hypertension, Stage 1	140–159	or	90–99
Hypertension, Stage 2	≥160	or	≥100

* See *Blood Pressure Measurement Techniques* (reverse side)
Key: SBP = systolic blood pressure DBP = diastolic blood pressure

Diagnostic Workup of Hypertension

- Assess risk factors and comorbidities.
- Reveal identifiable causes of hypertension.
- Assess presence of target organ damage.
- Conduct history and physical examination.
- Obtain laboratory tests: urinalysis, blood glucose, hematocrit and lipid panel, serum potassium, creatinine, and calcium. Optional: urinary albumin/creatinine ratio.
- Obtain electrocardiogram.

Assess for Major Cardiovascular Disease (CVD) Risk Factors

- Hypertension
- Obesity (body mass index ≥30 kg/m²)
- Dyslipidemia
- Diabetes mellitus
- Cigarette smoking
- Physical inactivity
- Microalbuminuria, estimated glomerular filtration rate <60 mL/min
- Age (>55 for men, >65 for women)
- Family history of premature CVD (men age <55, women age <65)

Assess for Identifiable Causes of Hypertension

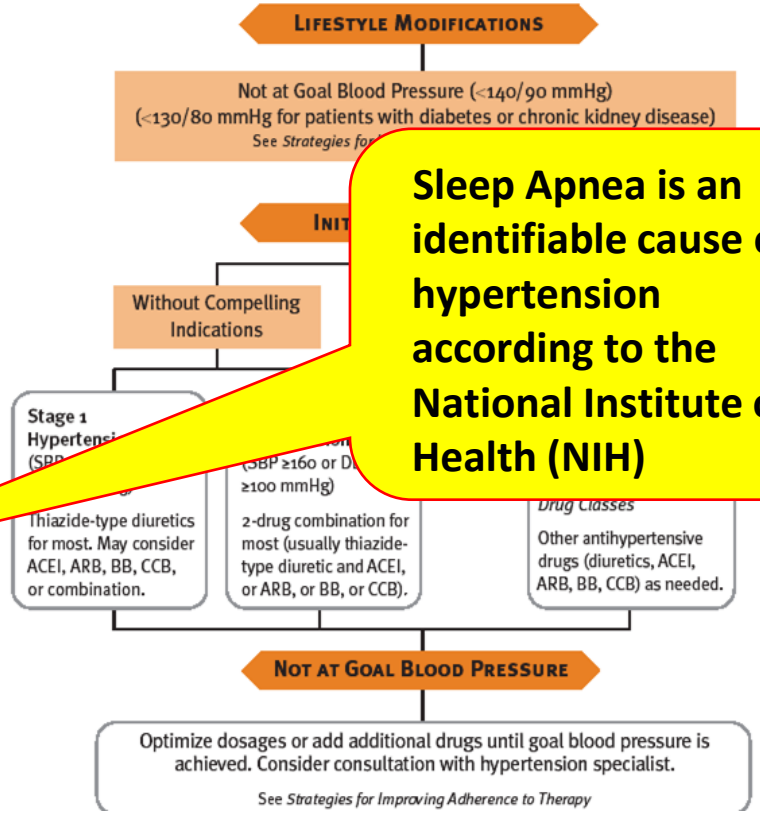
- Sleep apnea
- Drug induced/related
- Chronic kidney disease
- Primary aldosteronism
- Renovascular disease
- Cushing's syndrome or steroid therapy
- Pheochromocytoma
- Coarctation of aorta
- Thyroid/parathyroid disease

TREATMENT

Principles of Hypertension Treatment

- Treat to BP <140/90 mmHg or BP <130/80 mmHg in patients with diabetes or chronic kidney disease.
- Majority of patients will require two medications to reach goal.

Algorithm for Treatment of Hypertension



Sleep Apnea is an identifiable cause of hypertension according to the National Institute of Health (NIH)

CMHC
Cardiometabolic Health Congress

www.cardiometabolichealth.org

Foundations of Cardiometabolic Health Certification Course

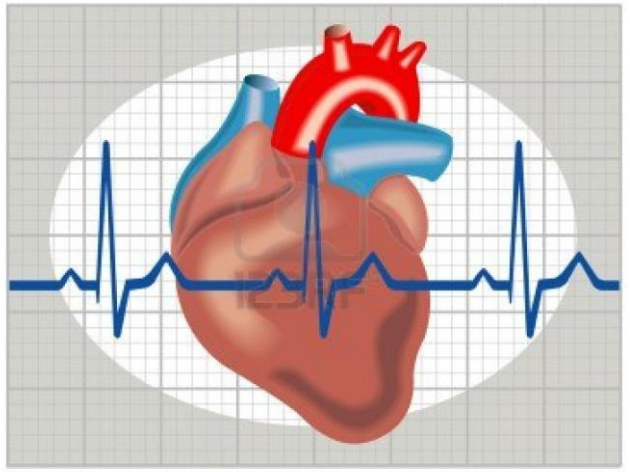
Certified Cardiometabolic Health Professional (CCHP)

OSA & Arrhythmias

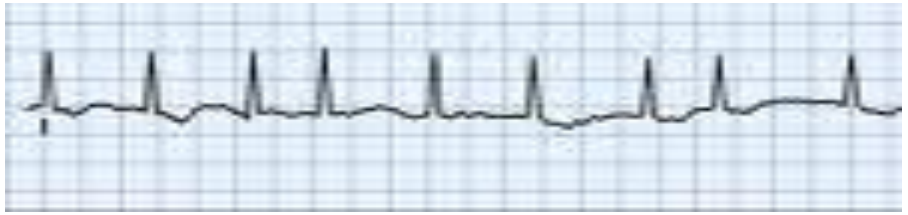
Lee A. Surkin, MD, FACC, FCCP, FASNC, FAASM
Founder, American Academy of Cardiovascular Sleep Medicine
President, Empire Sleep Medicine

Arrhythmias

- Increased risk with worsening OSA
- Occur in 50% of OSA patients
- Most common include PVCs, NSVT, Sinus Arrest, Bradycardia, Atrial Fibrillation
- Treating OSA improves
- Atrial Fibrillation is more difficult to convert to normal rhythm with untreated OSA
- Atrial Fibrillation ablation has high failure rate in untreated OSA patients

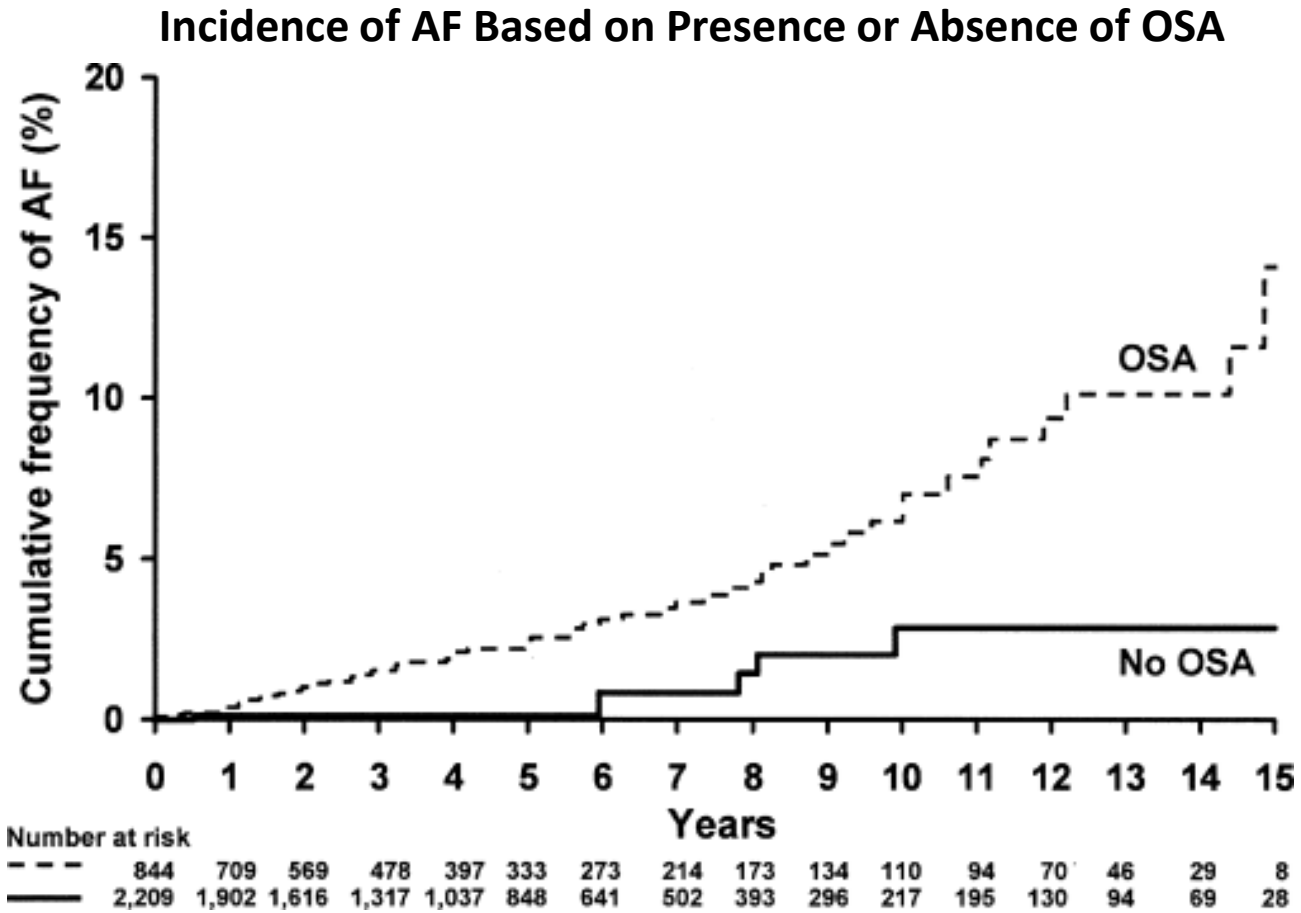


Atrial Fibrillation



- Obesity and hypoxemia are independent predictors of AFib in pts < 65
- 82% recurrence of Afib if OSA untreated after cardioversion
- 50% of pts presenting for cardioversion have OSA (30% in general cardiac population)
- Mechanisms: LA stretch more common in OSA, recurrent hypoxemia, significant catecholamine swings, arousals

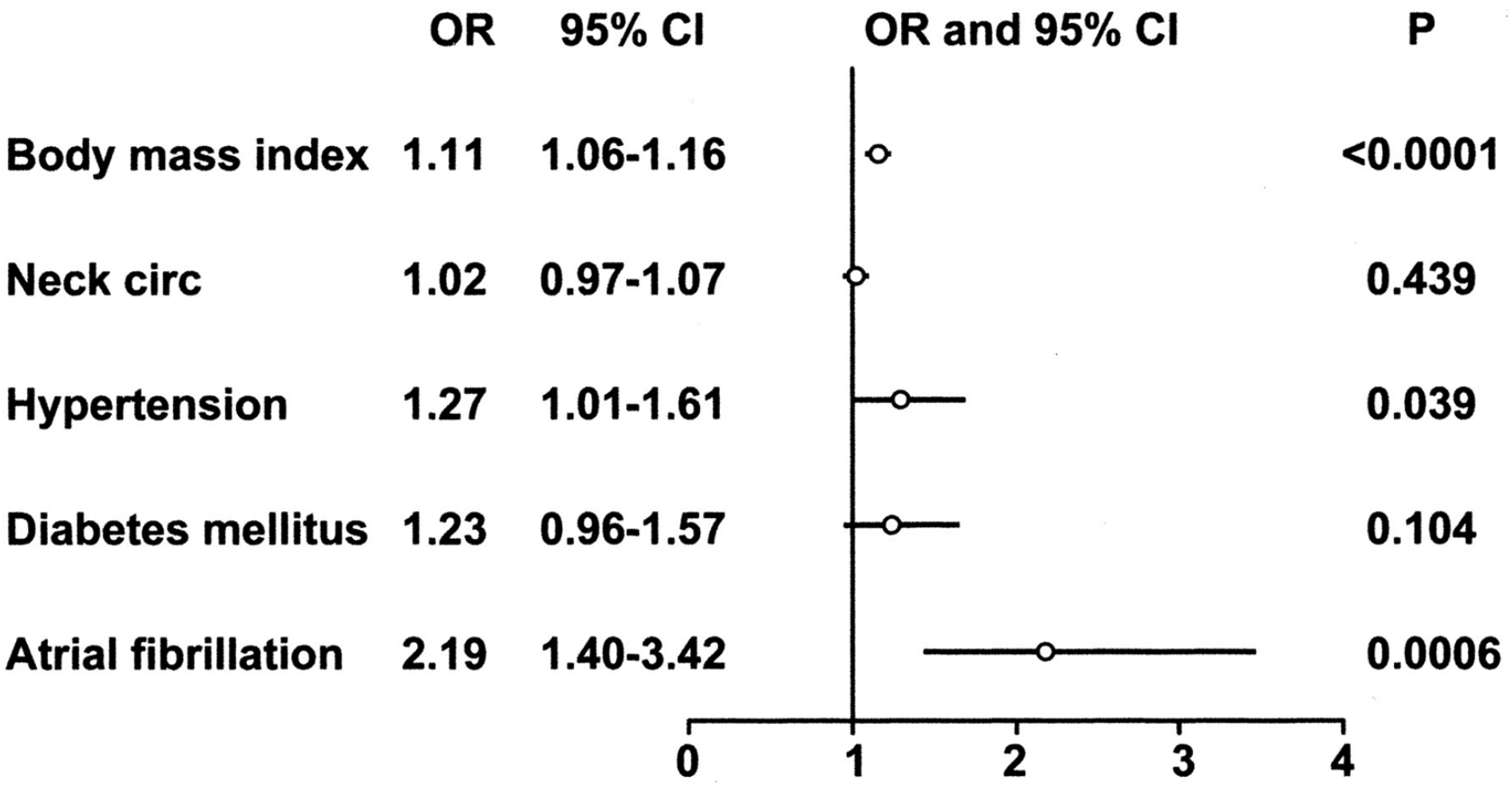
Atrial Fibrillation and OSA



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

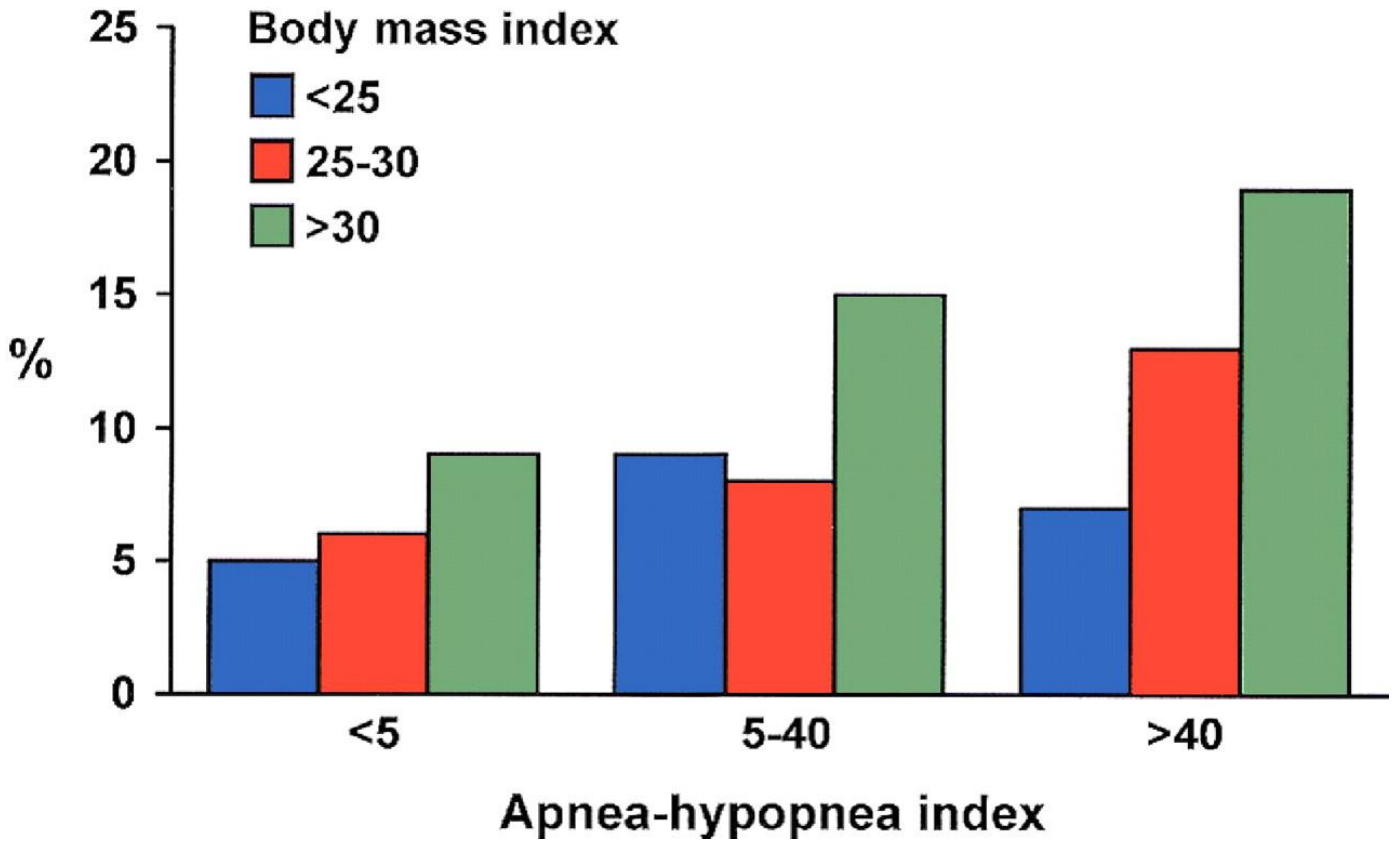
Gami AS, et al. J Am Coll Cardiol 2007; 49:565-571.

Adjusted OR and 95% CI for Association Between AF and OSA



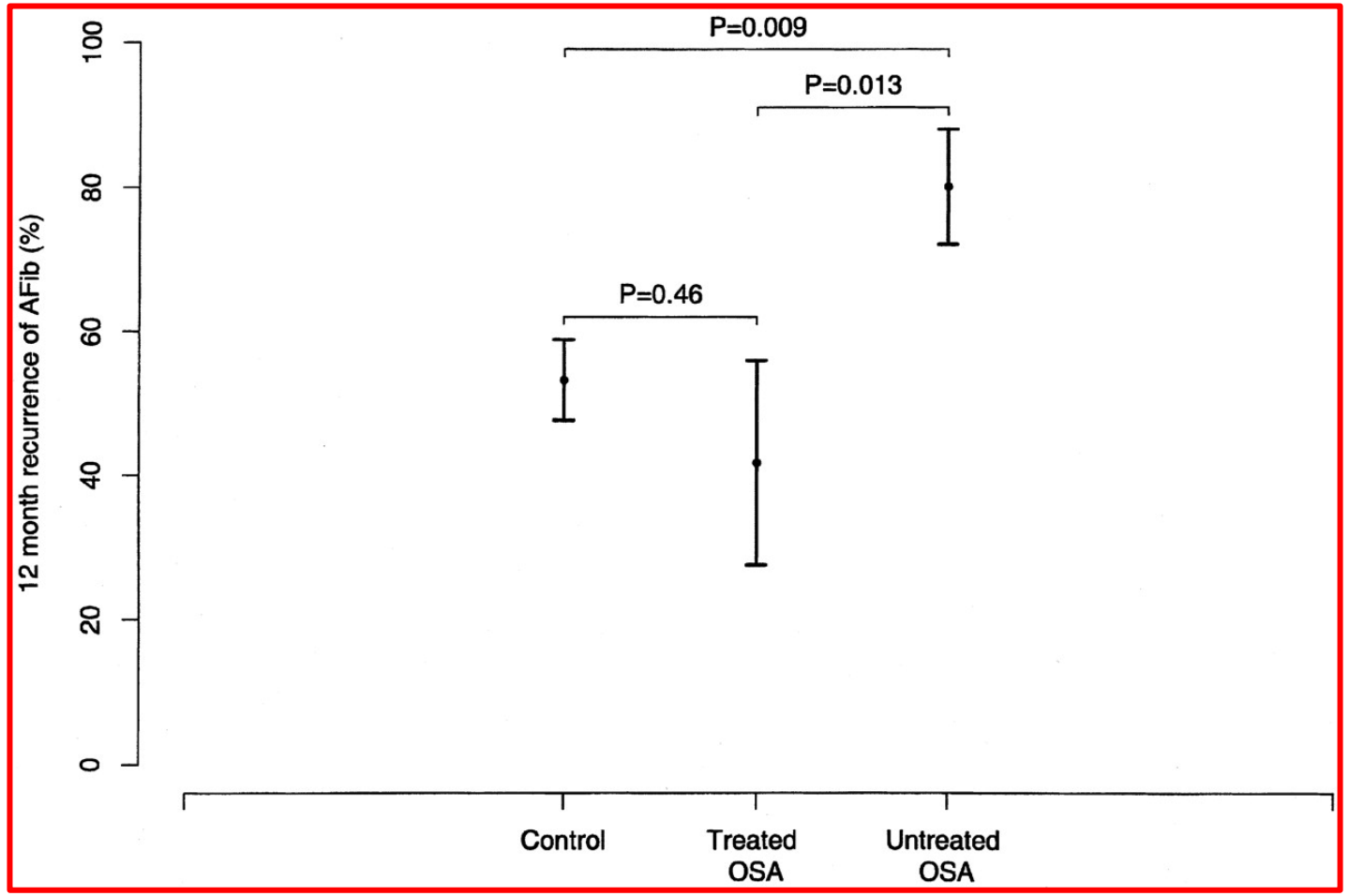
Gami, A. S. et al. Circulation 2004;110:364-367

Incidence of AF Based on the Severity of OSA and Obesity



Gami, A. S. et al. J Am Coll Cardiol 2007;49:565-571

Recurrence of AF at 12 months comparing patients with treated and untreated OSA



Kanagala, R. et al. Circulation 2003;107:2589-2594

Case Study:

70-year-old male referred for a syncopal episode

Cardiac HPI

- While moving furniture, bent over to pick up a chair, became dizzy and passed out
- No associated chest pain, palpitations, SOB, incontinence or seizure activity
- Regained consciousness and felt back to baseline

Sleep History

- Awakens refreshed
- Denies snoring
- Intermittent EDS
- Denies morning headaches
- No witnessed apneas
- Denies waking choking or gasping
- Epworth: 8/24

Past Medical History

- HTN
- Hyperlipidemia
- Gout
- Morbid Obesity

Physical Exam

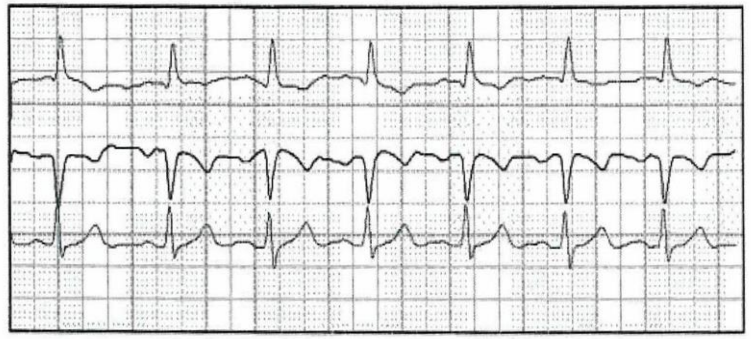
- BP: 154/87
- HR: 72
- RR: 18
- Wt: 274
- BMI: 41.7
- Unremarkable except for 2/6 SEM base, trace pitting edema lower extremities

Cardiac Evaluation

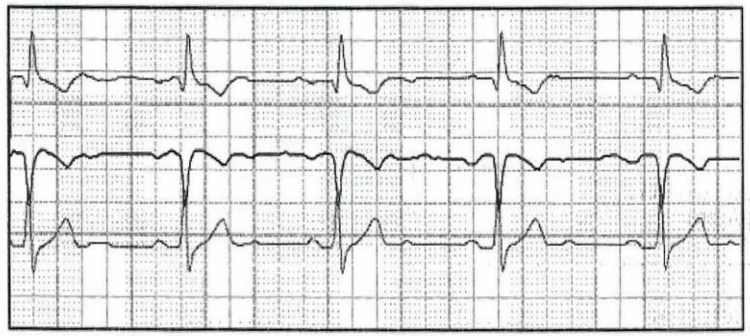
- Nuclear Stress Test:
  - Normal with LVEF= 55-60%
- Echocardiogram:
  - Normal LV systolic function
  - LVEF= 55-60%
  - Grade 1 Diastolic Dysfunction
  - No significant valvular disease
- Carotid Ultrasound
  - Mild diffuse non-critical plaguing

Ambulatory Cardiac Telemetry

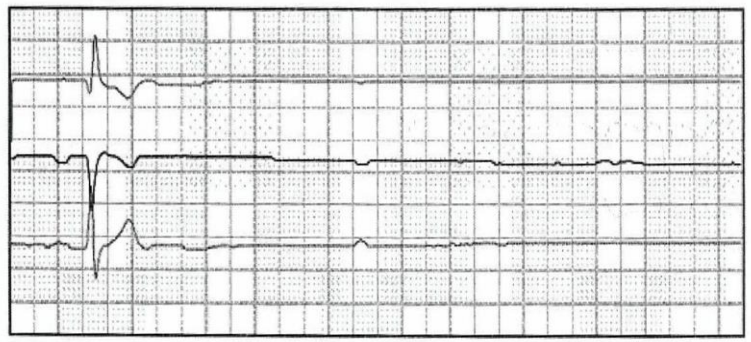
62



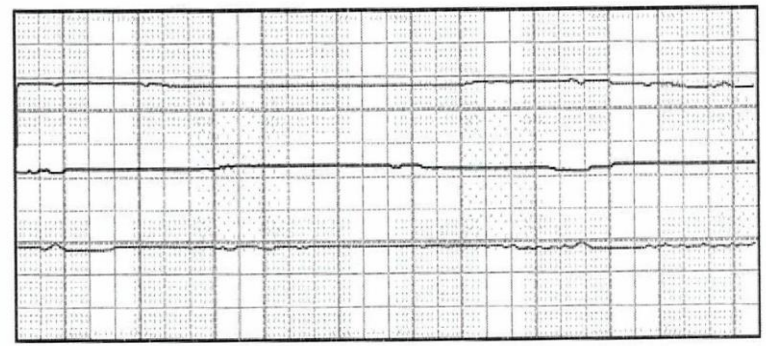
63



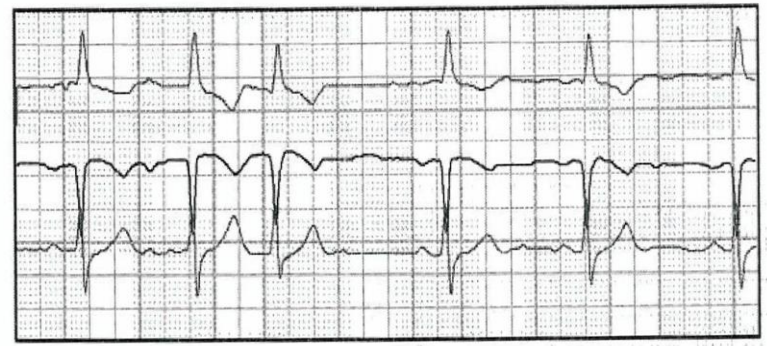
64



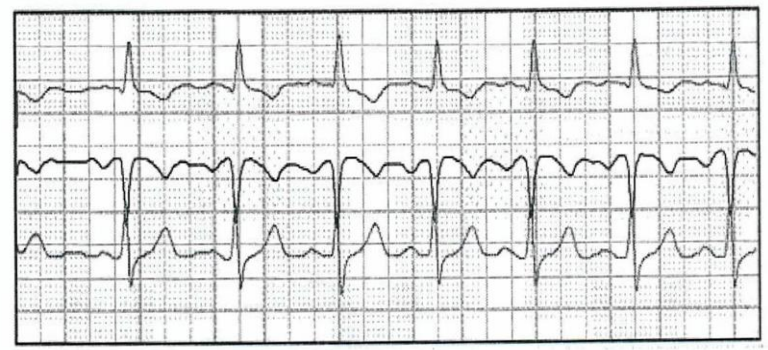
65



66



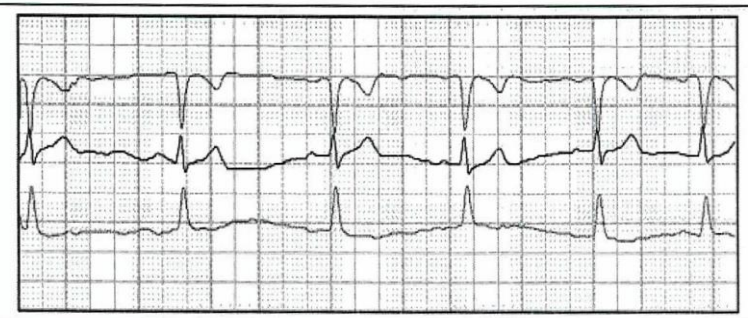
67



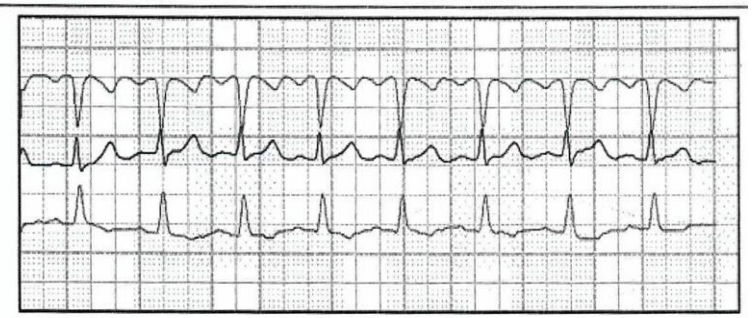
149

150

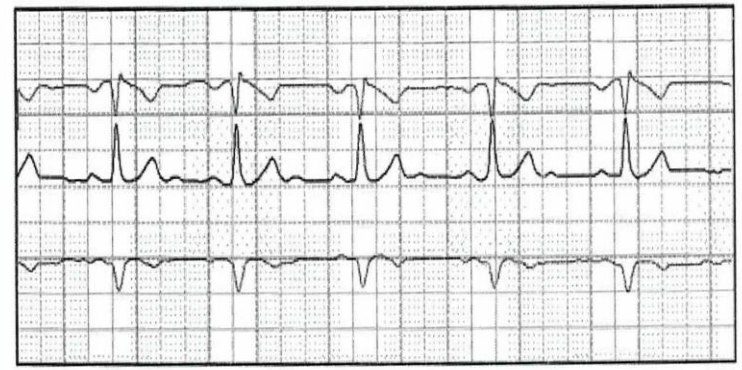
151



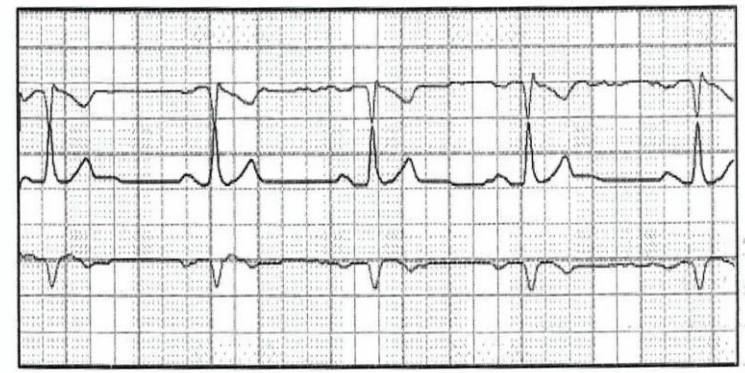
152



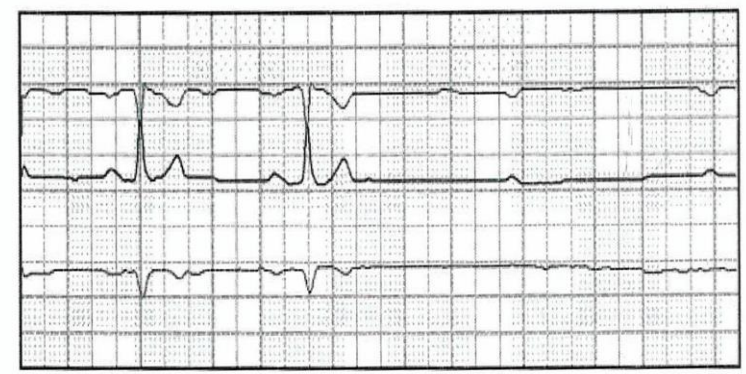
177



178

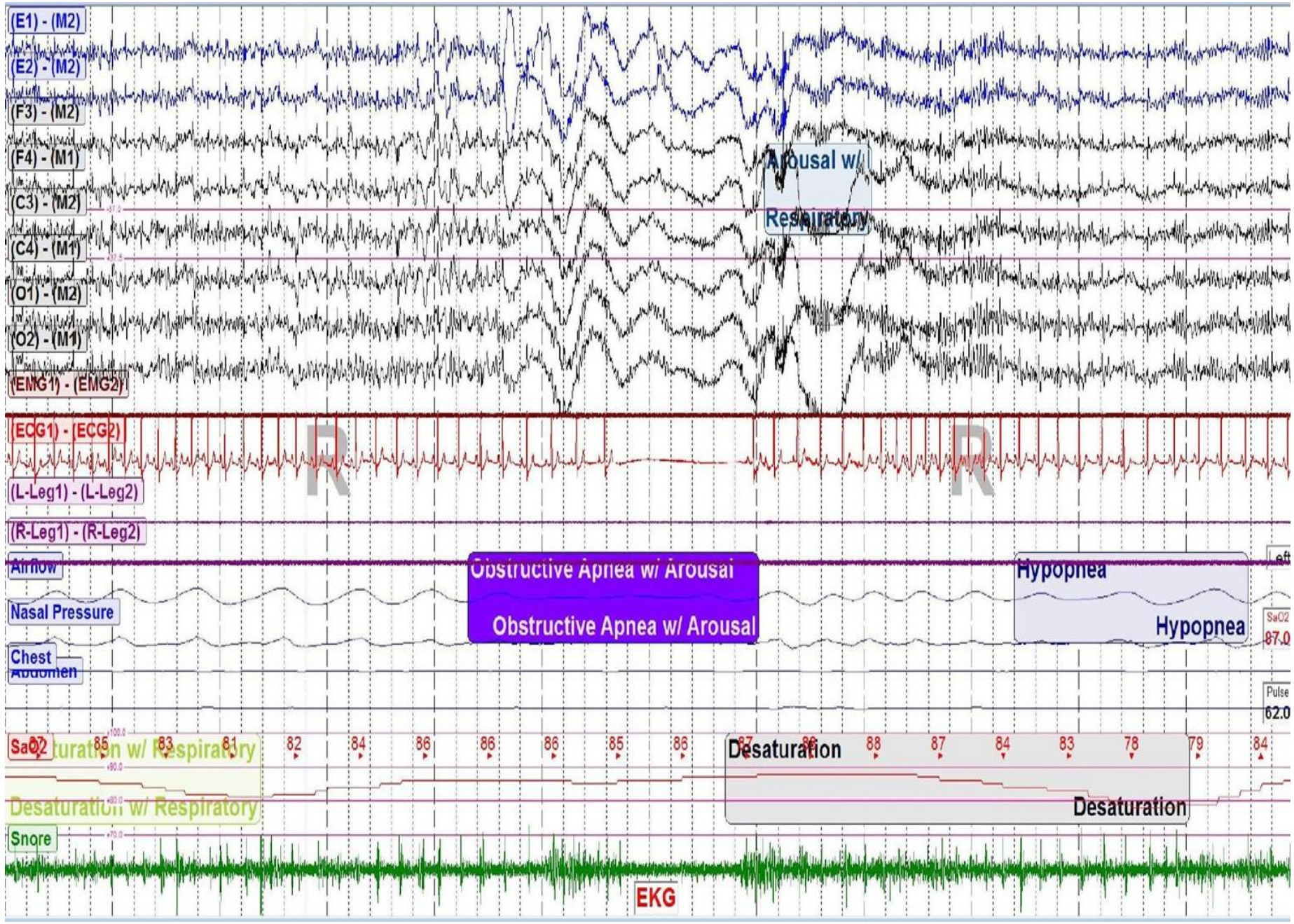


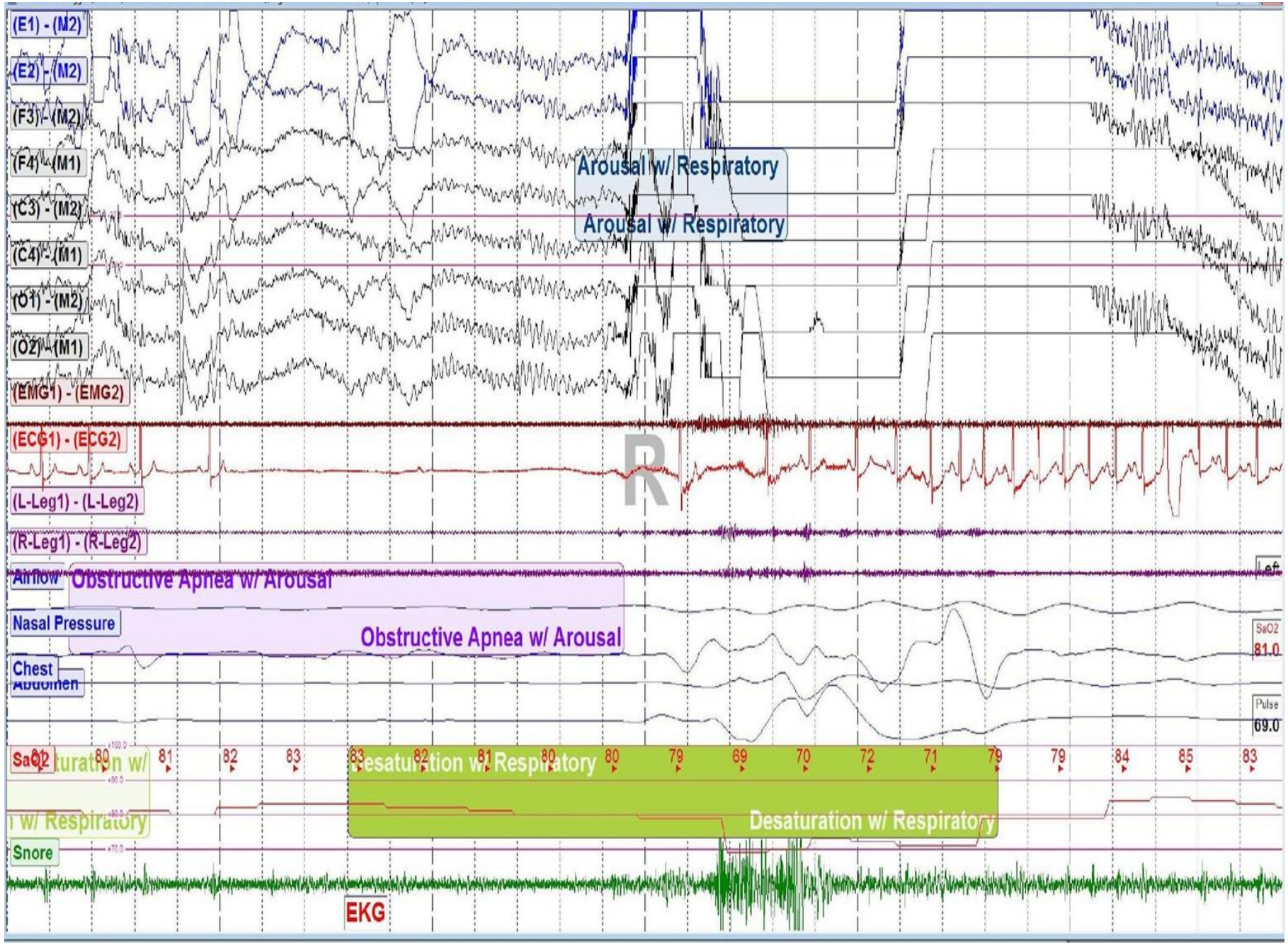
179



Sleep Evaluation

- Polysomnogram
  - Severe OSA with an AHI of 64.1 (REM AHI= 118.5).
    Marked brady-arrhythmias with complete heart block associated with respiratory events mostly in REM sleep. Desaturations to a low of 69%.


(E1) - (M2)
(E2) - (M2)
(F3) - (M2)
(F4) - (M1)
(C3) - (M2)
(C4) - (M1)
(O1) - (M2)
(O2) - (M1)
(EMG1) - (EMG2)
(ECG1) - (ECG2)
(L-Leg1) - (L-Leg2)
(R-Leg1) - (R-Leg2)
Airflow
Nasal Pressure
Chest
Abdomen
SaO2
Desaturation w/ Respiratory
Snore
Arousal w/
Respiratory
Obstructive Apnea w/ Arousal
Obstructive Apnea w/ Arousal
Hypopnea
Hypopnea
Desaturation
Desaturation
EKG
R
R
SaO2
87.0
Pulse
62.0


(E1) - (M2)
(E2) - (M2)
(F3) - (M2)
(F4) - (M1)
(C3) - (M2)
(C4) - (M1)
(O1) - (M2)
(O2) - (M1)
(EMG1) - (EMG2)
(ECG1) - (ECG2)
(L-Leg1) - (L-Leg2)
(R-Leg1) - (R-Leg2)
Airflow
Nasal Pressure
Chest
Abdomen
SaO2
Snore
EKG
Arousal w/ Respiratory
Arousal w/ Respiratory
R
Obstructive Apnea w/ Arousal
Obstructive Apnea w/ Arousal
Desaturation w/ Respiratory
Desaturation w/ Respiratory
SaO2
81.0
Pulse
69.0
80 81 82 83 83 82 81 80 80 79 69 70 72 71 79 79 84 85 83

Management

- CPAP titration optimized OSA resulting in no further episodes of asystole in the sleep lab
- Strict adherence to PAP therapy endorsed by patient
- Follow up 30-day ambulatory cardiac monitoring did not reveal recurrent arrhythmias

CMHC
Cardiometabolic Health Congress

www.cardiometabolichealth.org

Foundations of Cardiometabolic Health Certification Course

Certified Cardiometabolic Health Professional (CCHP)

OSA & Congestive Heart Failure

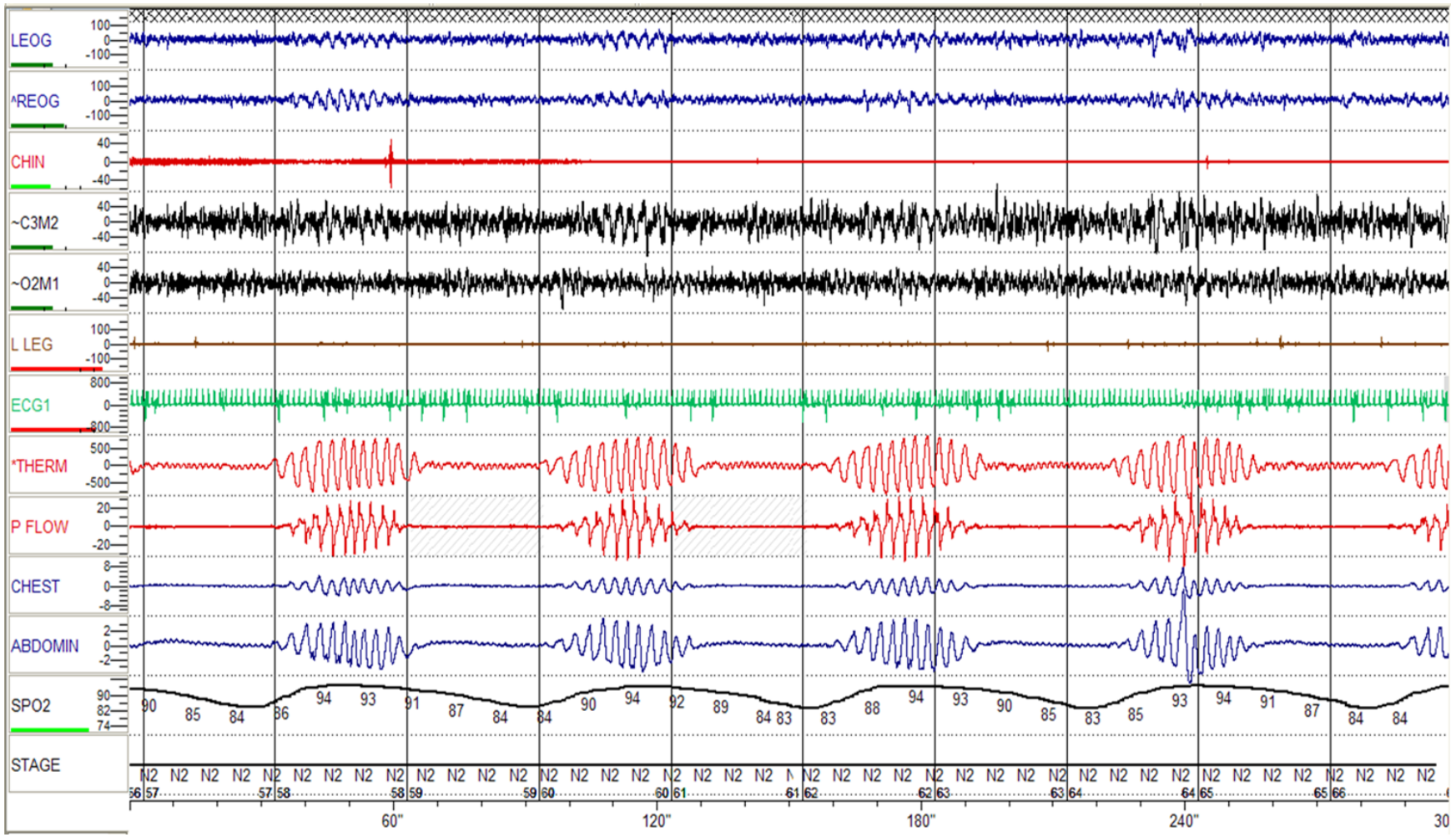
Lee A. Surkin, MD, FACC, FCCP, FASNC, FAASM
Founder, American Academy of Cardiovascular Sleep Medicine
President, Empire Sleep Medicine

Congestive Heart Failure (HFrEF and HFpEF)

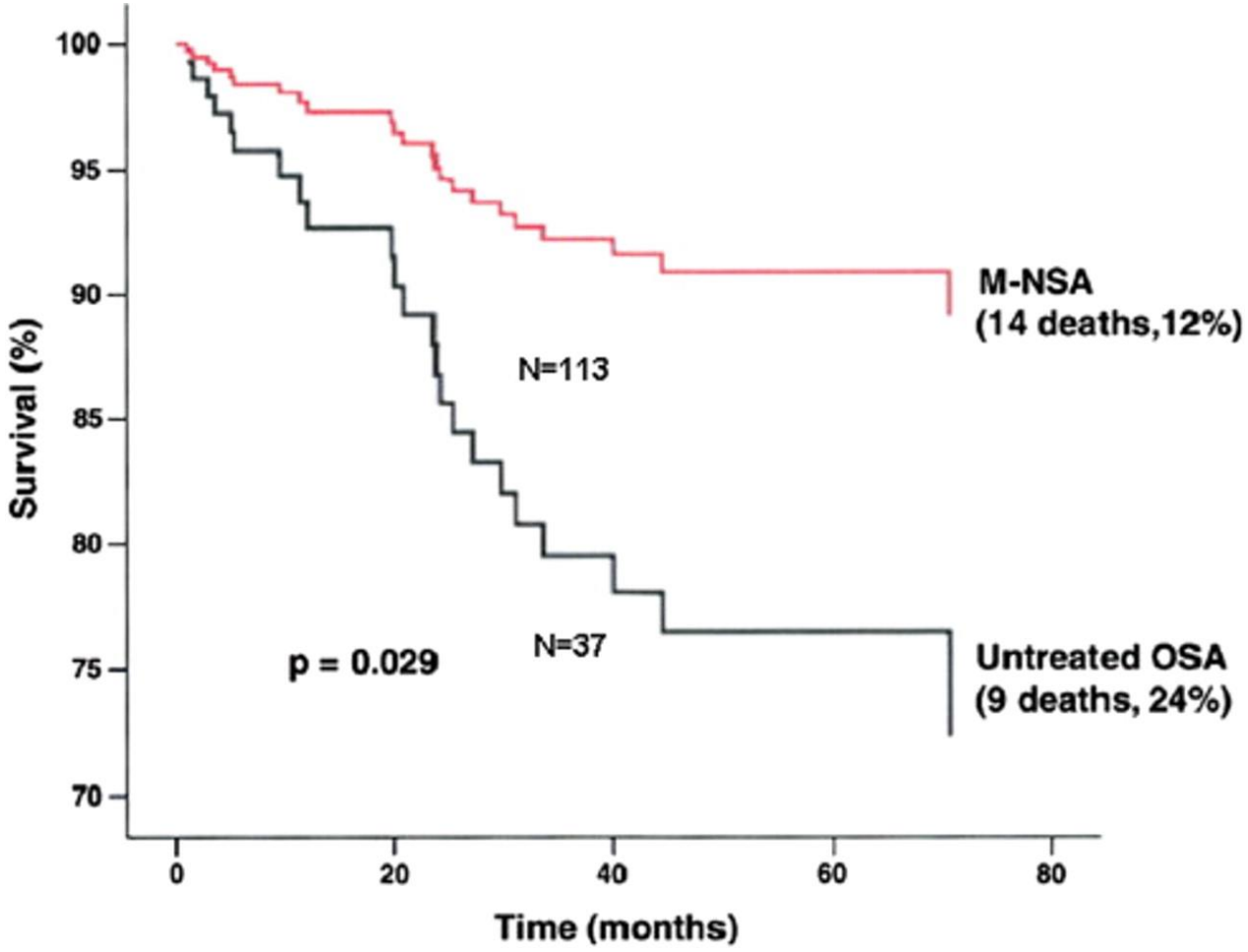
- 50-75% of CHF patients have OSA- according to a study by Oldenburg et al Eur J Heart Fail 2007;9:251-257
- Untreated moderate or severe OSA (AHI>15) and CHF is associated with increased mortality risk
- Cross-sectional data from the SHHS showed the presence of OSA with an AHI ≥11 to be associated with a 2.38 relative increase in the likelihood of having HF, independent of confounding factors
- Central Sleep Apnea (CSA) increases as HFrEF worsens and is associated with an increased mortality risk

Javaheri S et al. JACC 2007;49:2028-2034

Hunter-Cheyne-Stokes Breathing (HCSB)



CHF Survival in Normal or Mild Untreated OSA (AHI <15) vs Untreated OSA (AHI>15)



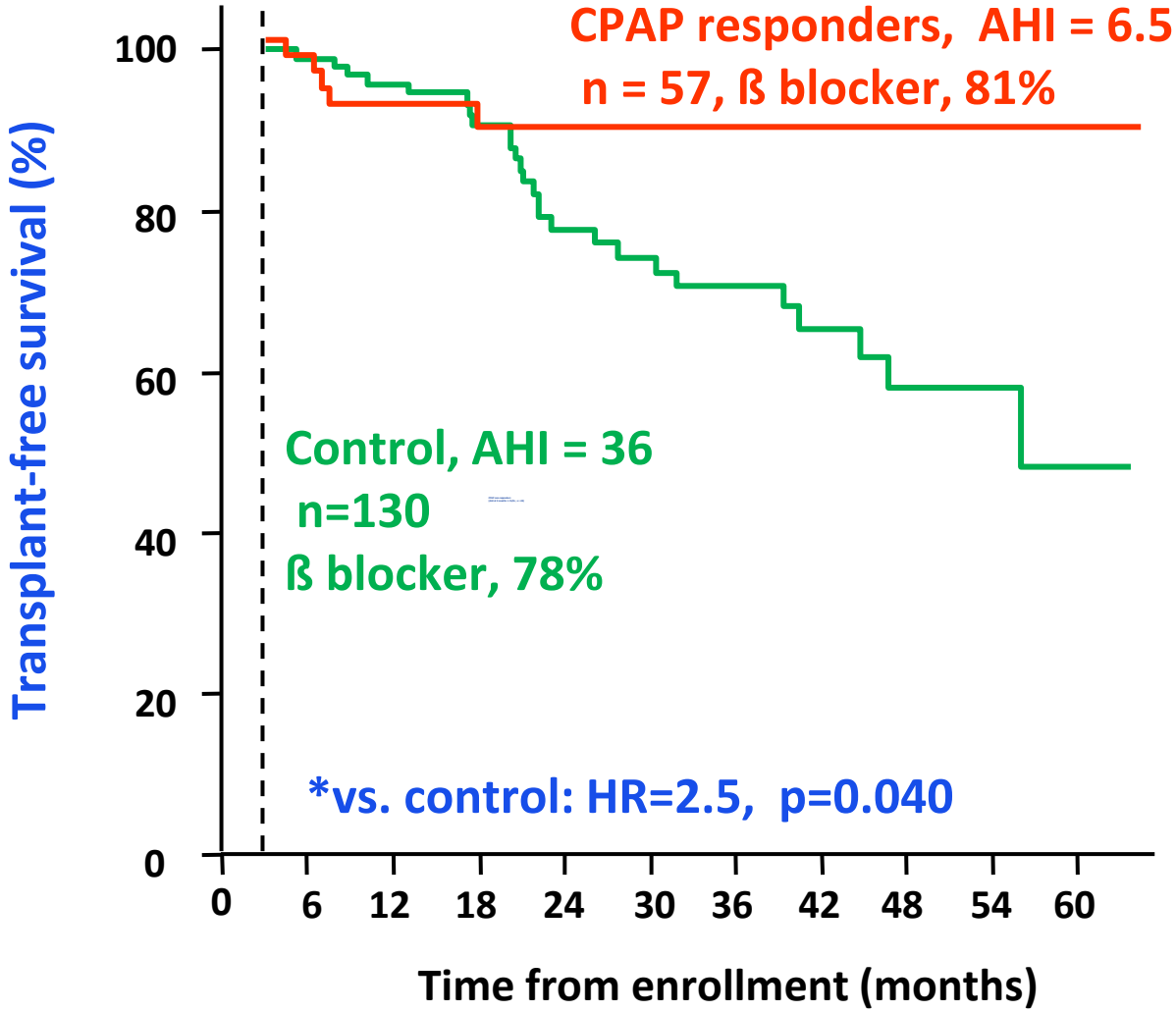
Kasai, T. et al. J Am Coll Cardiol 2011;57:119-127

CANPAP: Canadian Continuous Positive Airway Pressure for Central Sleep Apnea (CSA) and Heart Failure (HF) Trial

- Hypothesis: CPAP improves survival without cardiac transplantation in patients with CSA and heart failure
- Medical therapy optimized
- 258 patients enrolled with HF and CSA
- Randomly assigned to CPAP or no CPAP and followed for 2 years
- In CPAP group, AHI and Norepinephrine decreased and Mean SpO2, LVEF, 6-minute walk distance increased
- No difference in number of hospitalizations, QOL, ANP levels
- Early divergence in survival without transplant seen in control with divergence at 18 months favoring CPAP
- Overall event rates (death and heart transplant) did not differ

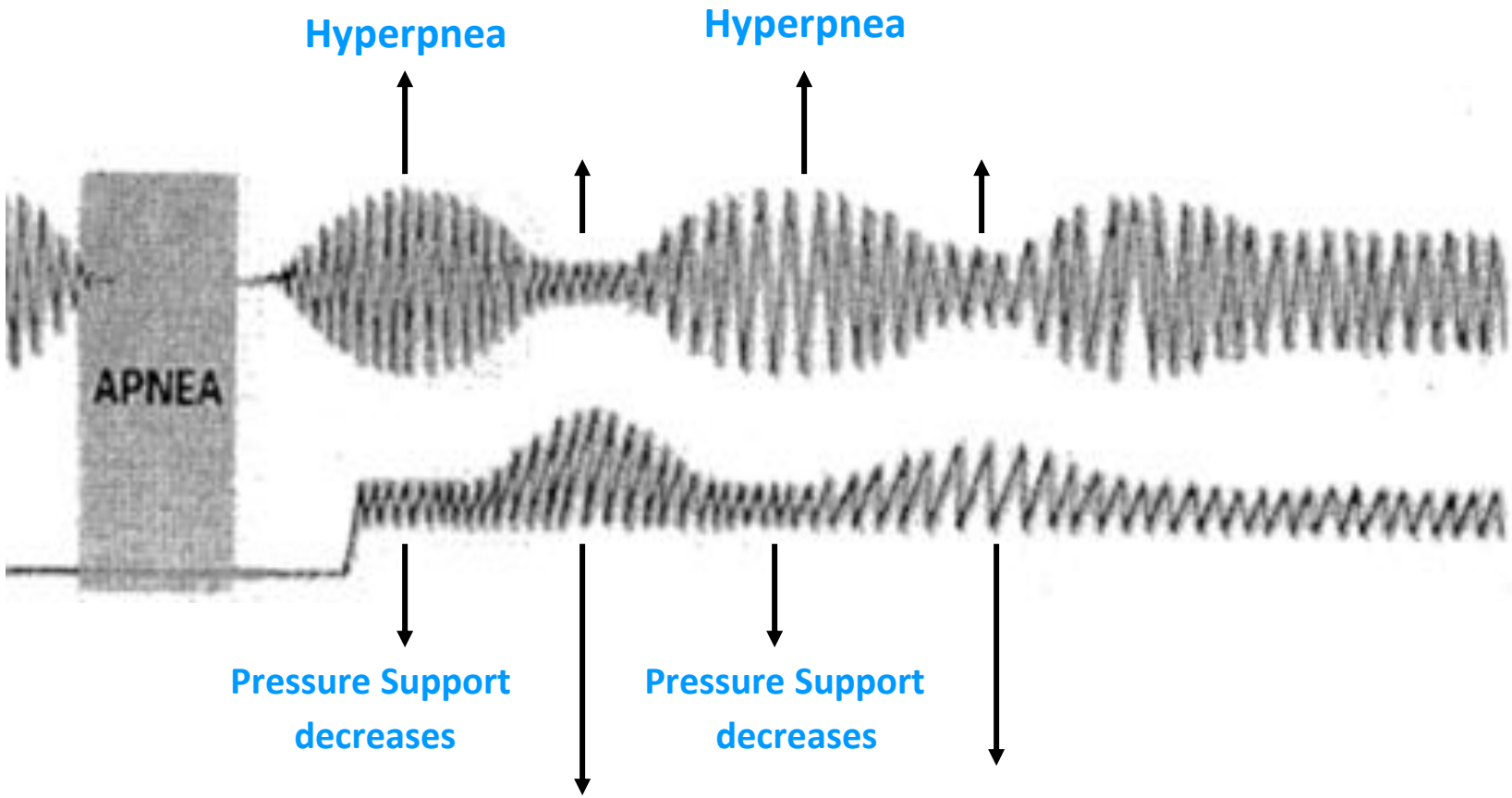
Bradley D, et al. NEJM 2005; 353:2025-2033

Post-hoc Analysis of the CANPAP RCT
Transplant-free Survival in HFrEF Patients



Artz, Circ, 2007

Adaptive Servoventilation (ASV) Corrects HCSB



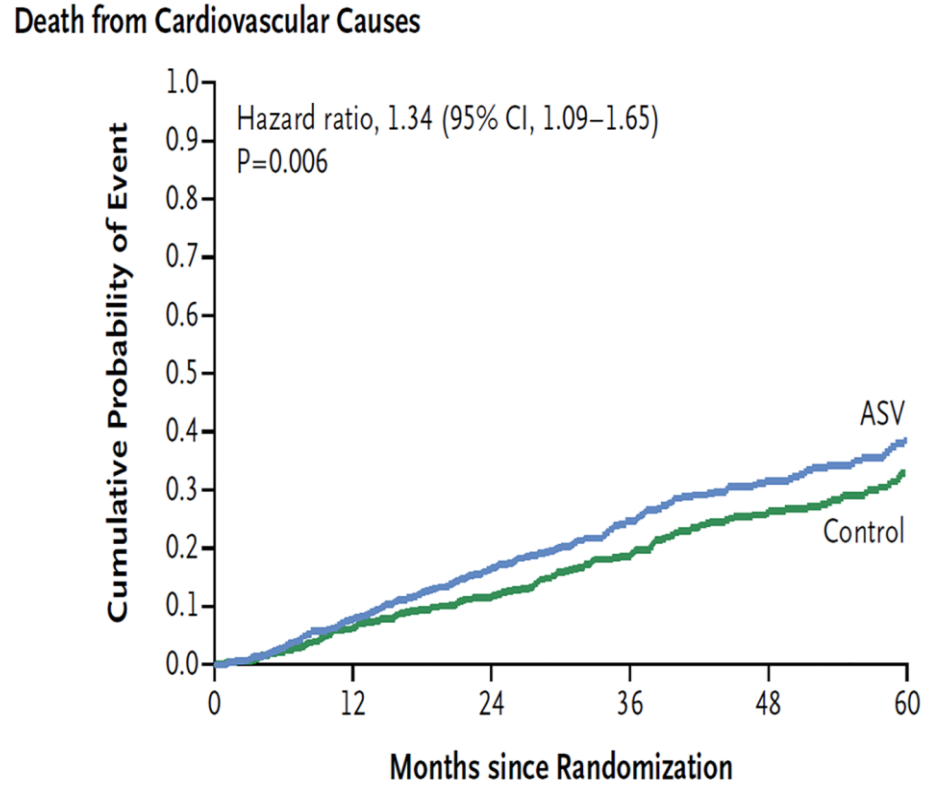
SERVE-HF

- 1300 patients with chronic HF with LVEF ≤45%
- NYHA class III or IV, or NYHA class II with ≥1 hospitalization for HF in the previous 24 months
- Subjects had predominant central SDB defined as an AHI ≥15 events/h with ≥50% central events and a central AHI ≥10 events/h
- Randomized to ASV or Usual Care

Cowie et al; NEJM, 2015

SERVE-HF: Results

- No statistically significant difference in the primary endpoint of time to all-cause mortality or unplanned hospitalization for worsening heart failure
- 2.5% absolute increased risk of annual CV mortality
- Study prematurely stopped due to mortality increase



No. at Risk						
Control	659	563	493	334	213	117
ASV	666	555	466	304	189	97

Cowie et al; NEJM, 2015

Phrenic Nerve Stimulation for the Treatment of Central Sleep Apnea: a Pooled Cohort Analysis

- Reduction in arousals by 14/hr
- Reductions in AHI (22/hr) and CAI (95% reduction)
- Improvement in sleepiness
- Improvement in QoL
- Improved oxyhemoglobin desaturation index
- Long-term outcomes announced 10/20/2020 and confirmed sustained benefit through 5 years

Costanzo, Respicardia Press Release Oct,2020

Acetazolamide for Obstructive and Central Sleep Apnea:

A Comprehensive Systematic Review and Meta-Analysis

- 28 studies, including 542 treatment subjects and 553 controls
- Acetazolamide doses 36-1000mg/day. Duration from 1-90 days (median 6days)
- Compared with controls, acetazolamide reduced the AHI by 37.7% (possibly secondary to respiratory stimulant effect)
- Reduction was similar in OSA vs CSA
- Improvements significantly greater with higher doses
- Acetazolamide improved SpO_2 nadir by +4.4% and sleep quality measures
- Benefits were short term. Long term efficacy has not been established but randomized trial is underway

Schmiki et al. CHEST. 2020

Ongoing CHF Trials

- ADVENT-HF: Heart failure patients with CSA or non-sleepy OSA treated with ASV

- LOFT-HF: Impact of Low-Flow Oxygen Therapy on Hospital Admissions and Mortality in Patients with Heart Failure and Central Sleep Apnea

Lyons OD, et al. Eur J Heart Fail 2017;19:579-587

CMHC
Cardiometabolic Health Congress

www.cardiometabolichealth.org

Foundations of Cardiometabolic Health Certification Course

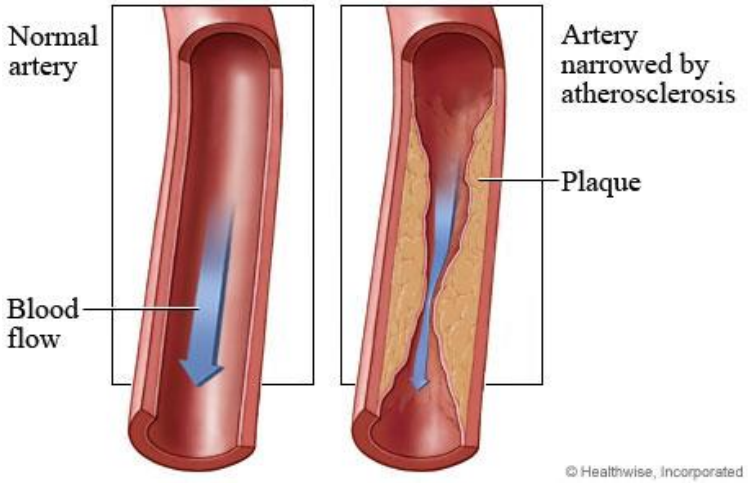
Certified Cardiometabolic Health Professional (CCHP)

OSA & Coronary Artery Disease

Lee A. Surkin, MD, FACC, FCCP, FASNC, FAASM
Founder, American Academy of Cardiovascular Sleep Medicine
President, Empire Sleep Medicine

Coronary Artery Disease

- OSA associated with increased risk of MI and CVA independent of other variables
- OSA linked to “Vulnerable Plaque” on CT
- OSA worsens other CV risk factors
- OSA not yet definitively considered an established cause of CAD
- More studies are urgently needed
- Possible Mechanisms…
  - Recurrent Hypoxia, Decreased Coronary Blood Flow
  - Arousal from Sleep, Increased Transmyocardial Pressure
  - Snoring mechanical forces, Systemic inflammation
- Daylight Savings Time effect



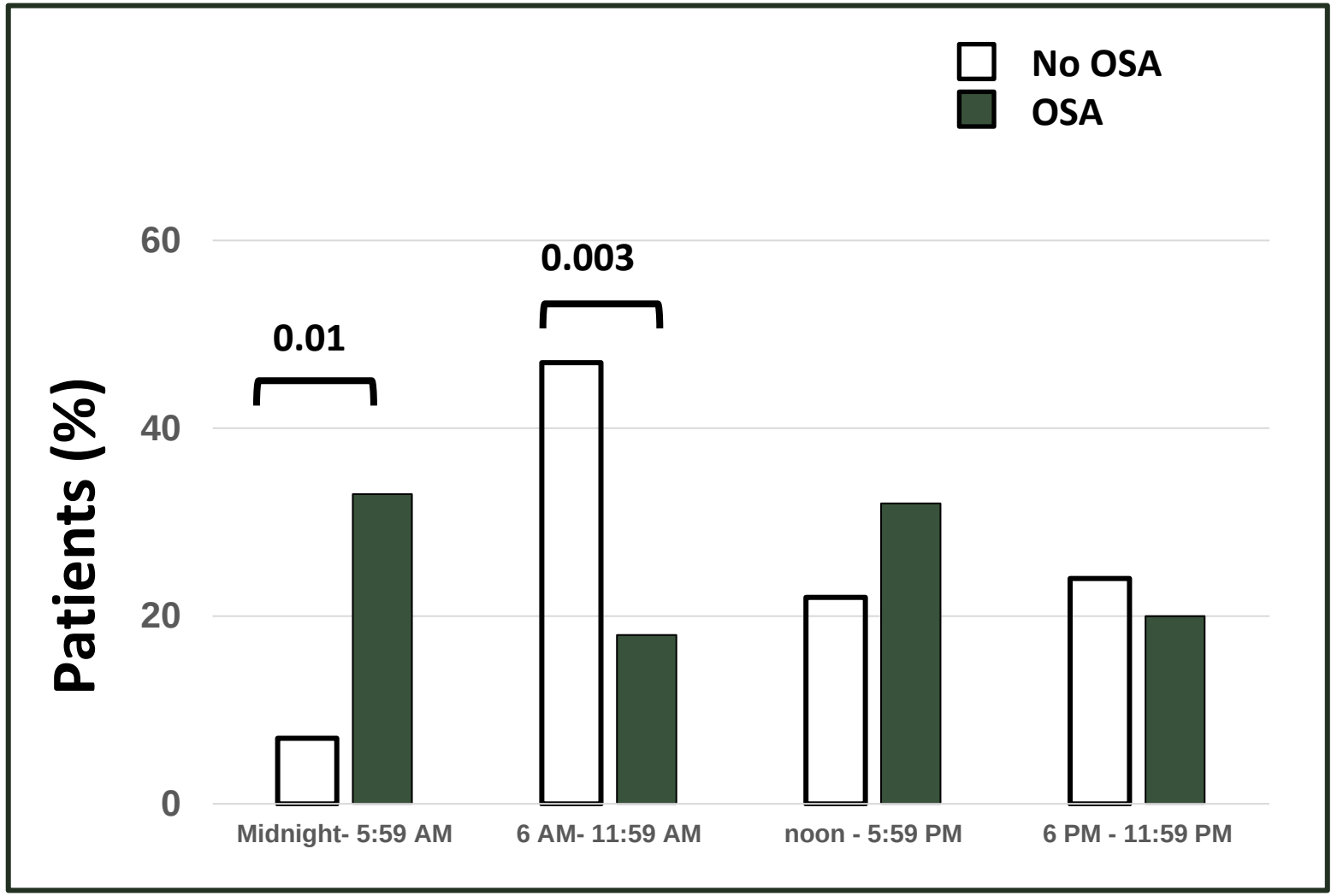
1 Marin Lancet 2005 2 Yaggi NEJM 2005 3 Arzt AJRCCM 2005

Daylight Saving Time and Acute Myocardial Infarction: A Meta-Analysis

- Meta-analysis evaluating the risk of AMI following DST transitions
- Seven studies including >115,000 subjects were included
- A significantly higher risk of AMI was observed during the two weeks following spring DST transitions
  - OR: 1.05; 95% CI 1.02–1.07
- American Academy of Sleep Medicine Position Statement:
  - Daylight savings time results in circadian misalignment
  - Associated with increased cardiovascular disease risk, metabolic syndrome and other health risks
  - Shifting to DST associated with increased cardiovascular morbidity
    - Increased risk of myocardial infarction, stroke, and hospital admissions for acute atrial fibrillation

Manfredini, et al. J. Clin. Med. 2019
Rishi, et al. J Clin. Sleep Med 2020

6-h Epochs of MI Occurrence



Sert Kuniyoshi, F. H. et al. J Am Coll Cardiol 2008;52:343-346

OSA and “Vulnerable Plaque” on CT

- Retrospective study by Dr. U. Schoepf from MUSC
- Measured coronary calcium (hard plaque) and degrees of non-calcified stenotic lesions (vulnerable or soft plaque)
- 95 patients studied: 49 with OSA (23 women) mean age 61, avg BMI 33. 46 without OSA (24 women) with similar characteristics
- No difference in hard plaque between two groups
- Total number of vessels with vulnerable plaque strongly correlated with OSA group (P=0.008) and the most stenotic lesions (P=0.0013)
- Study presented at 2010 Annual Meeting of Radiological Society of North America

Benefits of OSA Treatment in CAD

- Study by Milleron in Eur Ht Journal 2004
- 54 pts with CAD (>70% stenosis) and OSA (AHI>15)
- 25 treated with PAP or ENT surgery and 29 refused treatment
- Followed 4-10 years for MACE (Death, ACS, CHF hospitalization, Revascularization)
- Similar CAD treatments
- Treatment group had 6/25, 24% events. Untreated had 17/29, 58% (P<0.01)
- Treatment significantly reduced the risk of MACE

OSA/CAD: Four RCT

- ***Barbe et. al., JAMA, 2012***
- Peker et. al., AJRCCM, 2016 (RICCADSA Trial-Randomized Intervention with Continuous Positive Airway Pressure in CAD and OSA)
- McEvoy et. al, NEJM, 2016 (SAVE Trial-Sleep Apnea Cardiovascular Endpoints)
- Sanchez-de-la-Torre et. al., The Lancet Respiratory Medicine, 2019 (ISAACC Trial)

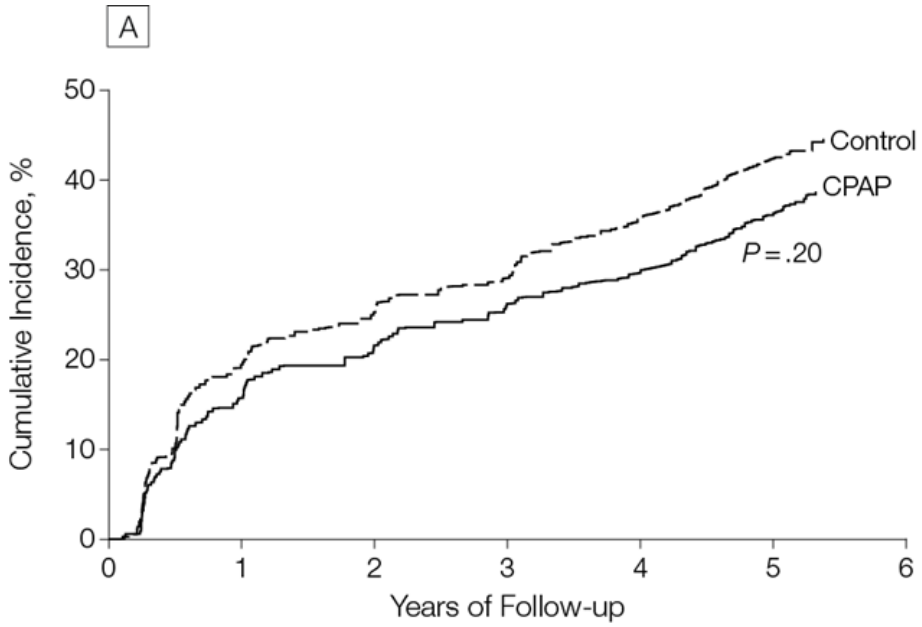
Effect of CPAP on the Incidence of HTN and CV Events in Patients with OSA

- 723 consecutive patients without known CVD (50% HTN) with AHI >=20 and ESS <10; 357 in CPAP group, 366 with usual care
- Mean age 52, BMI 31, 85% male
- AHI median 42 (29-59), SaO2<90% in 8% (2-22.8%)
- Primary outcome: Effect of CPAP treatment on incidence of HTN or CV events
- Secondary outcome: Association between the incidence of HTN or CV events and severity of OSA assessed by AHI and O2 desaturation
- Median F/U 4 years

Barbe F et al. JAMA 2012 May 23;307(20):2161-8

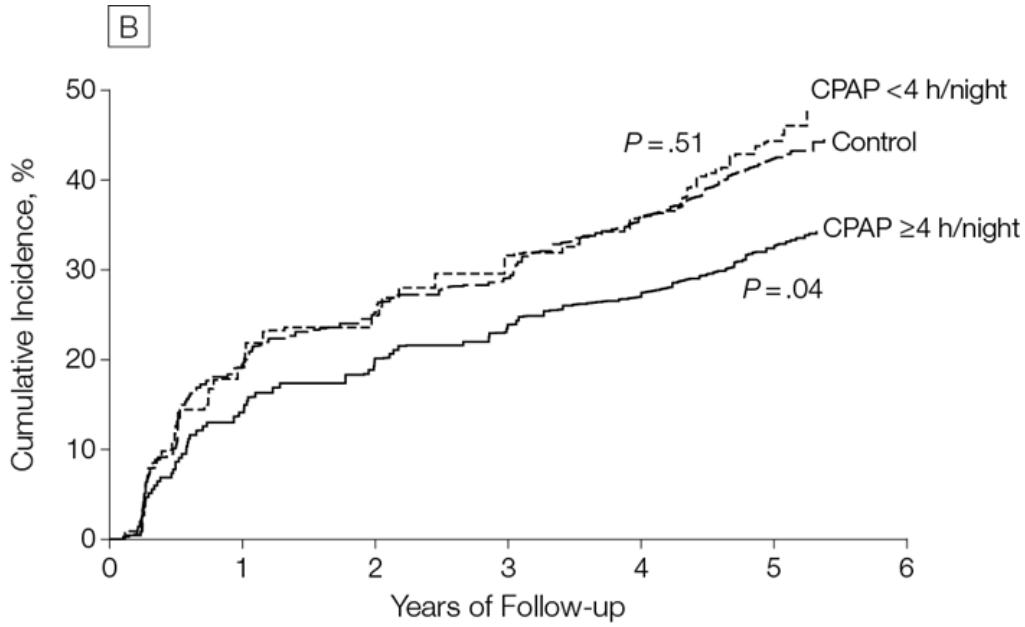
Results: No significant difference in treated group compared to control.

Post-hoc analysis on right shows benefit in adherent patients.



No. at risk

Control	366	264	234	206	134	10
CPAP	357	271	247	217	148	16



No. at risk

Control	366	264	234	206	134	10
CPAP <4 h/night	127	79	72	56	41	3
CPAP ≥4 h/night	230	192	175	161	107	13

Barbe F et al. JAMA 2012 May 23;307(20):2161-8

Effect of CPAP on the Incidence of HTN and CV Events in Patients with OSA: Summary & Implications

- This study suggests that in patients with OSA and *without daytime sleepiness*, CPAP compared with usual care did not result in a statistically significant reduction in the incidence of hypertension or cardiovascular events.
- A post hoc analysis suggested that CPAP treatment may reduce the incidence of hypertension or cardiovascular events in patients with CPAP adherence of 4 h/night or longer.
- The disease severity assessed by the AHI and time with SaO2 less than 90% was not related to the incidence of hypertension or cardiovascular events. However, patients with worse oxygen saturation at night and with CPAP adherence of less than 4h/night showed a higher rate of hypertension or cardiovascular events than the control group

OSA/CAD: Four RCT

- Barbe et. al., JAMA, 2012
- ***Peker et. al., AJRCCM, 2016 (RICCADSA Trial-Randomized Intervention with Continuous Positive Airway Pressure in CAD and OSA)***
- McEvoy et. al, NEJM, 2016 (SAVE Trial-Sleep Apnea Cardiovascular Endpoints)
- Sanchez-de-la-Torre et. al., The Lancet Respiratory Medicine, 2019 (ISAACC Trial)

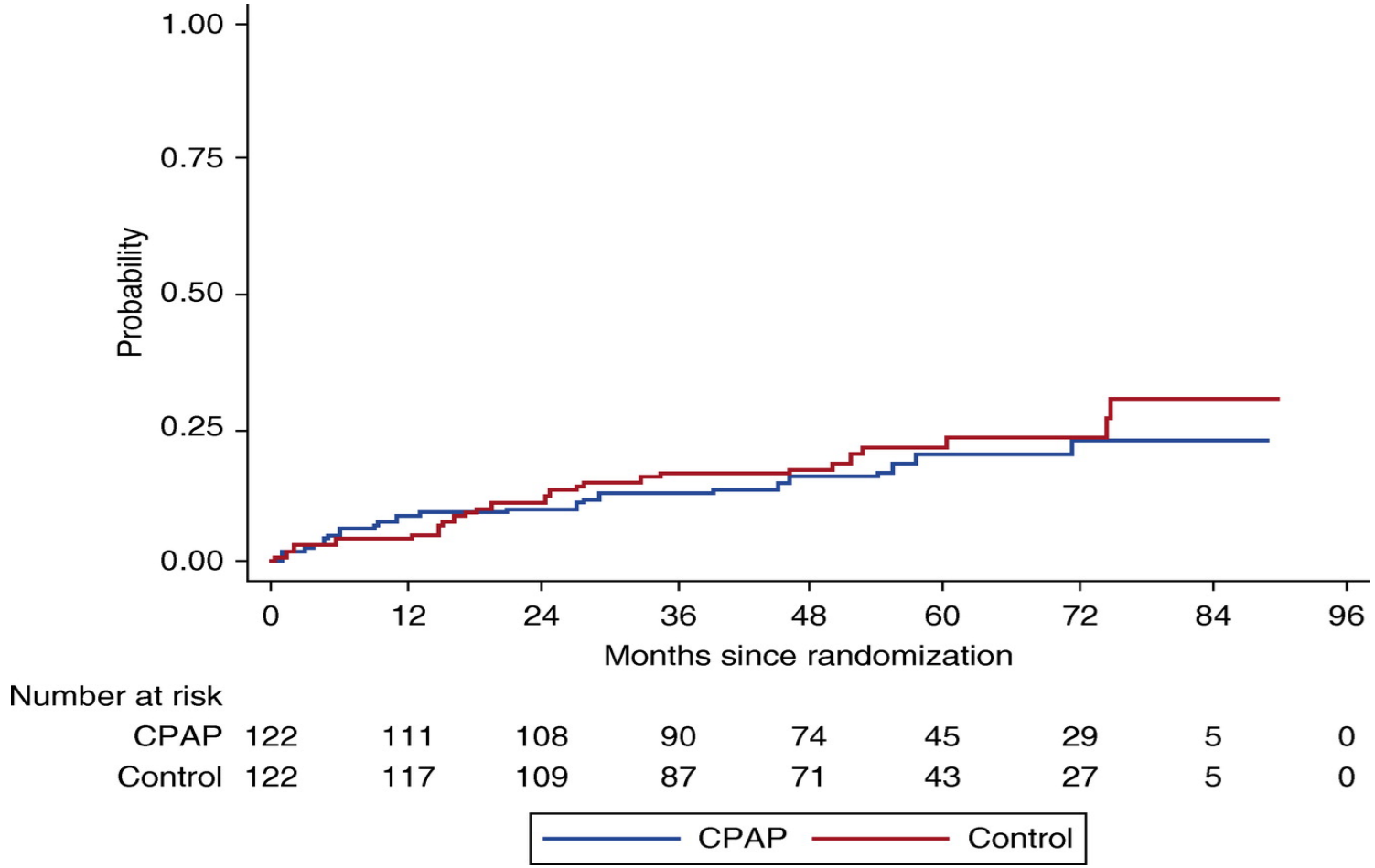
Effect of Positive Airway Pressure on CV outcomes in CAD patients with non-sleepy OSA: The RICCADSA Trial

- 244 patients with established CAD and/or Cerebrovascular disease
- Age 66 y; 85% men, BMI 28
- HTN 70%, Acute MI 53%, CABG 27%, PCI 22%, DM 28%
- ODI 17; AHI 28 by PSG
- Primary endpoint: First event of repeat revascularization, MI, stroke, or CV mortality

(Single center, prospective, randomized controlled, open-label, blinded trial)

Peker et al. AJRCCM, 2016;194:613-620

Cumulative Incidences of the Composite Endpoint in the Intention-to-Treat Population



Am J Respir Crit Care Med, 2016
http://www.atsjournals.org/doi/abs/10.1164/rccm.201601-0088OC

RICCADSA: Intention to Treat Data

- 17 returned CPAP within 1 month
- 13 returned CPAP within 1-3 months
- 8 returned CPAP within 3-6 months
- 7 returned CPAP within 6-12 months
- 4 returned CPAP within 12-24 months
- 1 lost to follow up
- 7 died

Total=57 patients

RICCADSA Trial Results and Conclusion

Results:

- Median follow up was 57 months
- Incidence of primary endpoint did not differ in treated vs. control (18% vs. 22%, P=0.449)

Conclusion:

- Routine prescription of CPAP to CAD patients with ***non-sleepy*** OSA did not significantly reduce long-term adverse CV outcomes in intention-to-treat population

RICCADSA Trial Results Based on Adherence

Results:

- Significant difference in outcomes based on adherence; (6 events in CPAP >4 hours/night, 43 events in CPAP <4 hours/night). HR=0.29, CI=0.10-0.86 with covariate adjustments
- Incidence of composite endpoints; 2.31 (95% CI=0.96-5.54) per 100 person-years for CPAP > 4 hours/night vs. 5.32 (95% CI 3.96-7.15) per 100 person-years for CPAP < 4 hours/night or no CPAP

Conclusion:

- **There was a significant reduction in endpoints after adjustment for baseline comorbidities and adherence with treatment**

OSA/CAD: Four RCT

- Barbe et. al., JAMA, 2012
- Peker et. al., AJRCCM, 2016 (RICCADSA Trial-Randomized Intervention with Continuous Positive Airway Pressure in CAD and OSA)
- ***McEvoy et. al, NEJM, 2016 (SAVE Trial-Sleep Apnea Cardiovascular Endpoints)***
- Sanchez-de-la-Torre et. al., The Lancet Respiratory Medicine, 2019 (ISAACC Trial)

SAVE Trial (Sleep Apnea Cardiovascular Endpoints)

- 2687 ***non-sleepy*** patients with established CAD and/or Cerebrovascular Disease
- 81% men, BMI 29
- ODI=28; AHI=29 by HSAT (ApneaLink)
- RCT: Open labeled, CPAP or usual care
- Primary endpoint: Composite of death from any CV cause, MI, CVA, hospitalization for CHF, ACS

McEvoy RD, et al. NEJM 2016;375:919-931

SAVE Trial: CPAP use

- APAP initially set to the auto-mode for 1 week and thereafter set to the 90th percentile pressure
- First month usage: 4.4 +/- 2.2 hours per night
- 12 months: 3.5 +/- 2.4 hours per night
- Remained relatively stable thereafter with overall mean of 3.3 +/- 2.3 hours per night

SAVE Trial: Results

- The primary outcome, CV death; myocardial infarction (MI); stroke; hospitalization for HF, unstable angina, or transient ischemic attack, for CPAP + usual care vs. usual care: 17.0% vs. 15.4% (hazard ratio 1.10, 95% confidence interval 0.91-1.32); p = 0.34

- CV death: 1.9% vs. 1.5%, p=0.5

- MI: 3.1% vs. 2.9%, p=0.8

SAVE Trial: Overview

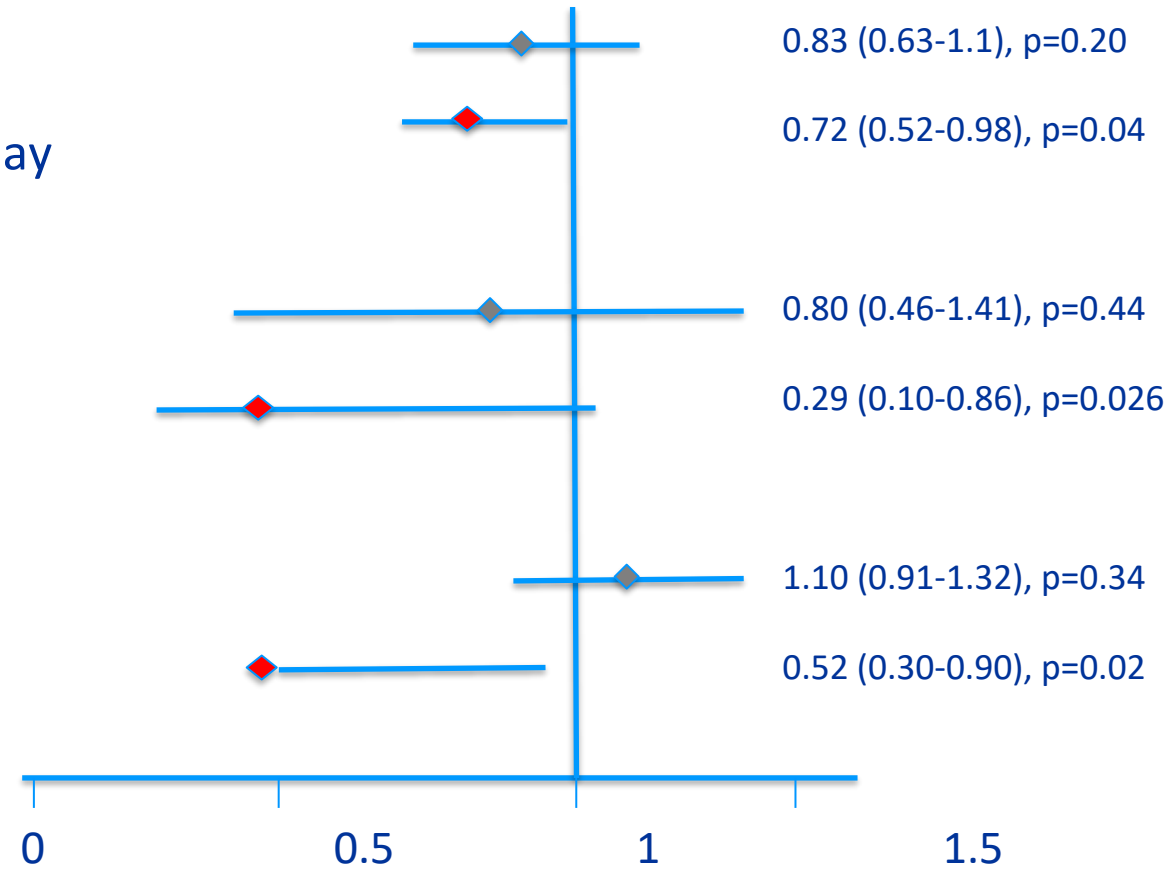
- CPAP as an addition to usual care is not superior to usual care alone for secondary prevention of CV events in patients with established CAD and CVD and moderate to severe OSA.
- CPAP did improve daytime sleepiness and health-related quality-of-life parameters.
- On adjusted propensity analyses, it appeared that there may be a benefit in patients using at least 4 hours of CPAP every night on average (mean in trial, 3.3 hours).

- Intention-to-treat analysis
- Adherence analysis (patients with CPAP adherence ≥ 4 hours/day

Barbe et al. (CPAP=358, Control=367) Follow-up: 4 yrs

Peker et al. (CPAP=122, Control=122) Follow-up: 4,7 yrs

McEvoy et al. (CPAP=1359, Control=1358) Follow-up: 3, 7 yrs

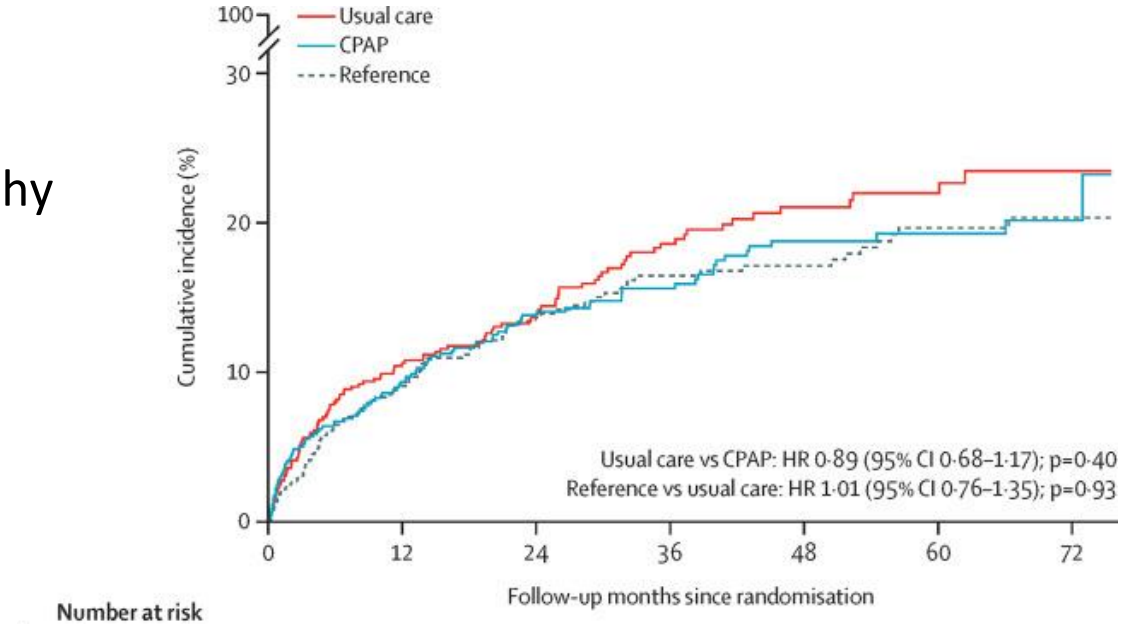


OSA/CAD: Four RCT

- Barbe et. al., JAMA, 2012
- Peker et. al., AJRCCM, 2016 (RICCADSA Trial-Randomized Intervention with Continuous Positive Airway Pressure in CAD and OSA)
- McEvoy et. al, NEJM, 2016 (SAVE Trial-Sleep Apnea Cardiovascular Endpoints)
- ***Sanchez-de-la-Torre et. al., The Lancet Respiratory Medicine, 2019 (ISAACC Trial)***

Effect of OSA and its Treatment with CPAP on the Prevalence of Cardiovascular Events in Patients with Acute Coronary Syndrome (ISAACC study)

- ISAACC study (Impact of Sleep Apnea syndrome in the evolution of Acute Coronary syndrome)
  - Spanish, multicenter, RCT of patients with ACS
- 2551 patients with ACS underwent respiratory polygraphy
  - 49.6% had OSA
  - Randomly assigned to CPAP or usual care
  - Followed up for a median of 3.35 years
- Cardiovascular events similar between groups
  - 16% *vs* 17%; HR – 0.89, p=0·40
  - 15% in those without OSA
  - **Mean CPAP use 2.78 h/night**
- OSA was not associated with an increase in cardiovascular events and treatment with CPAP did not significantly reduce events



Sanchez-de-la-Torre M, et al. Lancet Respir Med 2020;8:359-367

CPAP Adherence for Prevention of Major Adverse Cerebrovascular and Cardiovascular Events in OSA

- Meta-analysis - 5 trials with 943 CPAP users and 1,141 controls
- Primary outcome – composite of CVA, AMI, cerebrovascular or cardiac death
- CPAP use of at least 4 hours/night, compared with no CPAP therapy
  - Improved the primary composite outcome (RR, 0.68, P = 0.01)
  - CPAP improved cerebrovascular composite outcome (RR, 0.59, P=0.01)
  - No difference in the cardiac composite outcome
- Adequate use of CPAP (>4 h/d) associated with significant improvements in MACCEs (primarily CVAs)

Javaheri et al. AJRCCM, 2019

Sleep and Cardiovascular Disease

- Insufficient sleep duration and OSA clearly shown to increase cardiovascular disease, major adverse cerebrovascular and cardiovascular events (MACCEs), and mortality
- Intuitively, adequate treatment of OSA should improve cardiovascular outcomes
- Multiple studies demonstrated beneficial effects of PAP therapy
  - Largely limited to modest improvements in BP and Afib control
- 2012-2016 several RCTs failed to show CPAP reduces MACCEs
  - Limited by poor PAP adherence

Javaheri S, et al. JACC

CMHC
Cardiometabolic Health Congress

www.cardiometabolichealth.org

Foundations of Cardiometabolic Health Certification Course

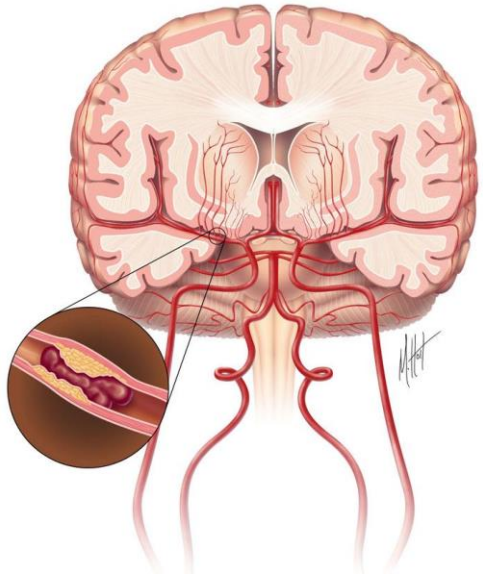
Certified Cardiometabolic Health Professional (CCHP)

OSA & Cerebrovascular Accident

Lee A. Surkin, MD, FACC, FCCP, FASNC, FAASM
Founder, American Academy of Cardiovascular Sleep Medicine
President, Empire Sleep Medicine

Cerebrovascular Accident

- 750,000 CVA Annually
- 72% of patients with CVA have OSA
- OSA precedes onset of CVA
- Results from similar CV causes of hypertension, inflammation, oxidation, etc
- Snoring associated with carotid disease
- OSA treatment difficult to assess secondary to adherence issues



Cerebrovascular Accident

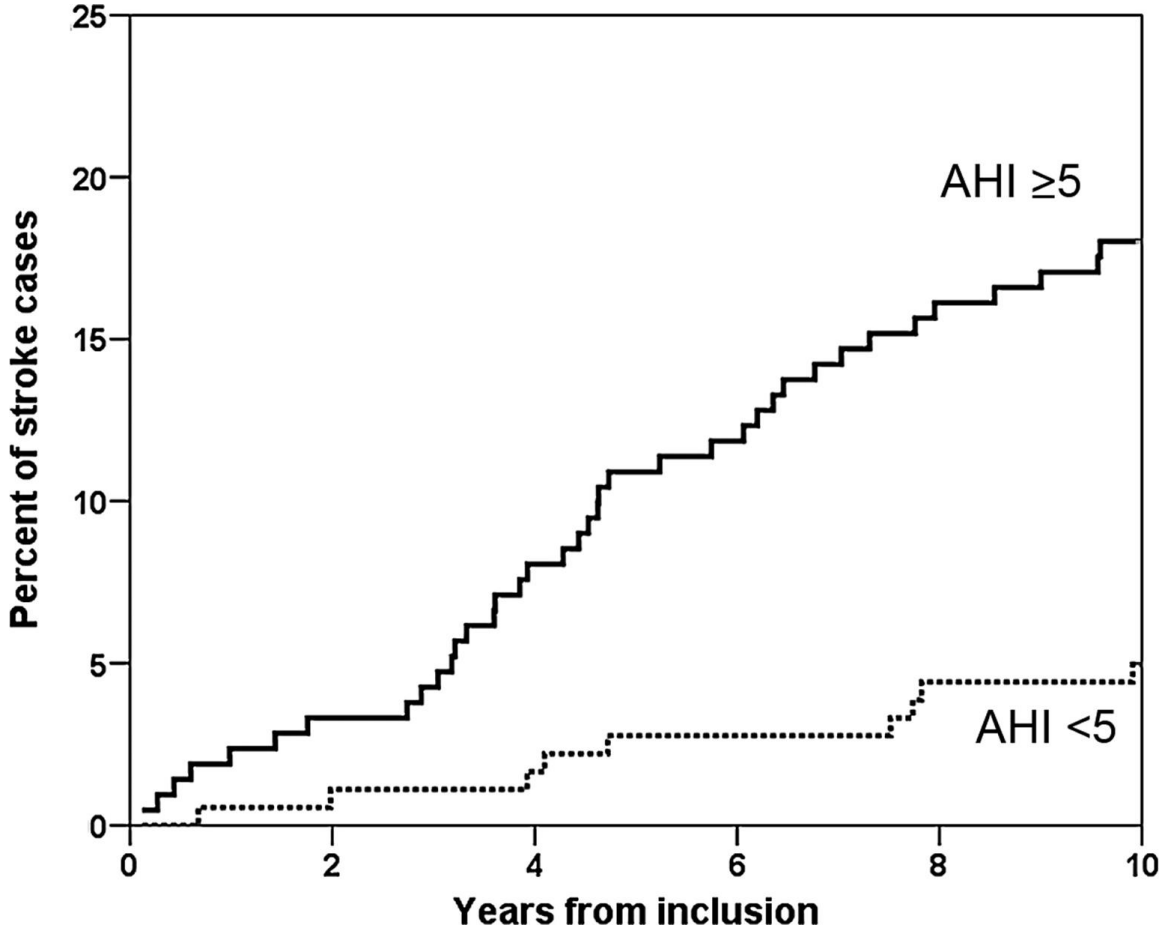
- Most commonly associated with obstructive sleep apnea (36-90% of patients)[1]
- Also associated with central sleep apnea (12-40%)
- Central SA has better outcome than obstructive[2]
- Severe central SA > 2 weeks with large CVA and cardiac dysfunction have poor outcomes[3]
- SA improves in 50% during recovery phase (mostly central SA improves)[4]

1Bassetti Sleep 1999 2Sahlin Arch Int Med 2008 3Wessendorf J Neurol 2000 4Parra AJRCCM 2000

CVA Mechanisms

- Endothelial dysfunction
- Coagulation
- Inflammation/Oxidation
- Metabolic/DM
- HTN
- Hypoxia/Hypercapnea

Cumulative Risk of CVA During 10 Years of Follow-up

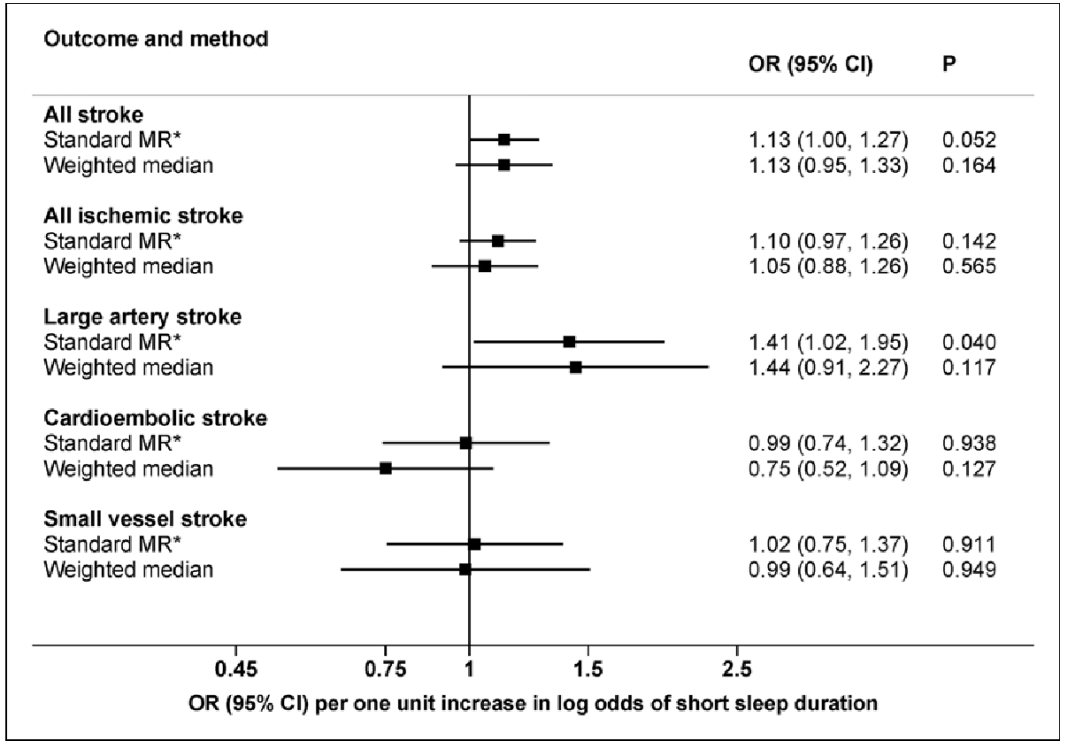


Valham, F. et al. Circulation 2008;118:955-960

Sleep Duration and Stroke

Prospective Cohort Study and Mendelian Randomization Analysis

- Prospective observational study, N=79,881 (Swedish Registers)
- Followed for incident stroke or death
- Mean follow-up 14.6 years (116,464 person-years)
- Long sleep (>9h) – increased risk of ischemic stroke (HR 1.14)
- Short sleep (<7h) – higher risk of intracerebral hemorrhage (HR 1.21)
- Modest effect size



Titova, et al. Stroke, 2020

Sleep Duration and Cardiovascular Health in a Representative Community Population

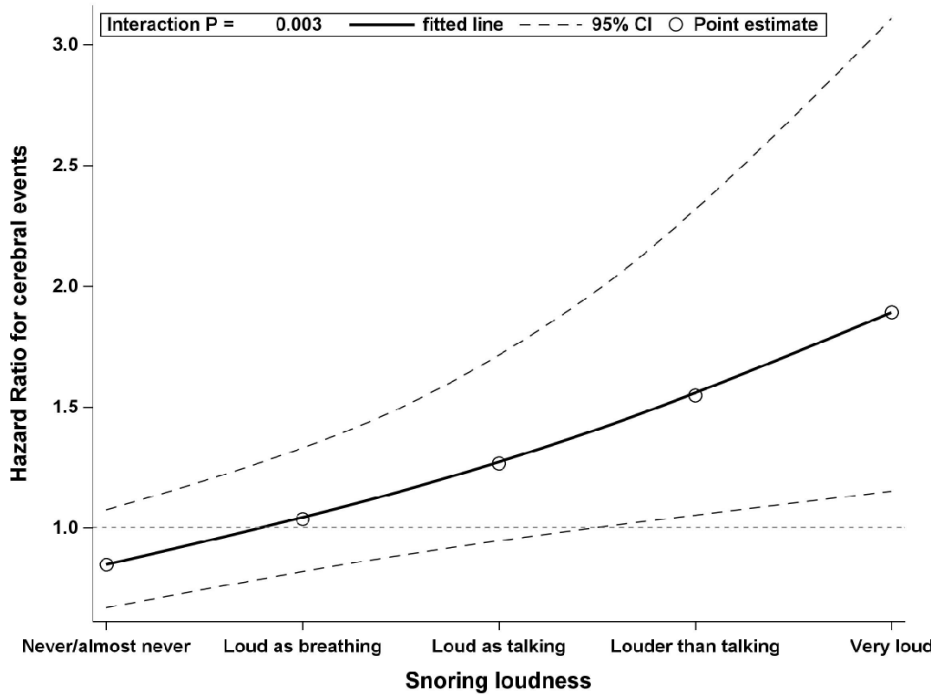
(from NHANES, 2005 to 2016)

- 32,152 patients completed sleep survey as part of National Health and Nutrition Examination Survey
- Identified all patients with HF, coronary artery disease, hypertension, hyperlipidemia, DM, and stroke from 2005 to 2016
- Data adjusted for multiple confounders
- Both short (<7 hours) and long (>9 hours) sleep duration associated with poor cardiovascular health
- Short sleep associated with higher prevalence of…
  - CVA (OR 1.45; 95% CI 1.23 to 1.70)
  - Heart Failure (OR 1.65; 95% CI 1.40 to 1.95)
- Long sleep duration was associated with a higher prevalence of…
  - CVA (OR 1.81; 95% CI 1.37 to 2.34)
  - Heart Failure (OR 1.47; 95% CI 1.08 to 1.97)

Am J Cardiol, 2020

Self-reported Snoring Patterns Predict Stroke Events in High-risk Patients With Obstructive Sleep Apnea: post-hoc analyses of the SAVE study

- Explored major CV events between those who reported snoring prior to PAP use vs those who denied snoring
- Snoring vibrations induce carotid artery endothelial damage in animal models
- Snorers w/ OSA had greater risks of cerebral but not cardiac events
  - Independent of CPAP treatment and AHI
  - Dose-dependent relationship
- Snoring frequency: HR 1.10, 95% CI 1.02-1.20, p=0.015
- Snoring loudness: HR 1.16, 95% CI 1.06–1.27, p=0.001



Li, et al. Chest, 2020

CMHC
Cardiometabolic Health Congress

www.cardiometabolichealth.org

Foundations of Cardiometabolic Health Certification Course

Certified Cardiometabolic Health Professional (CCHP)

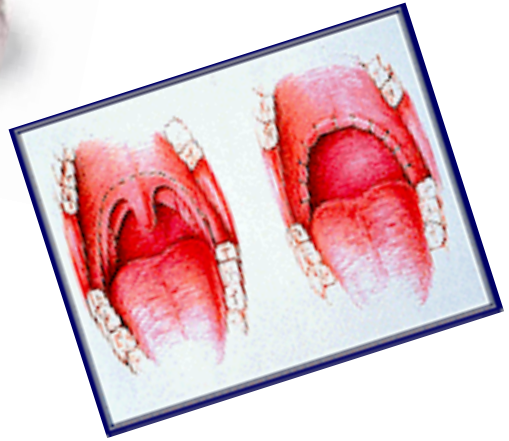
Treatment Options

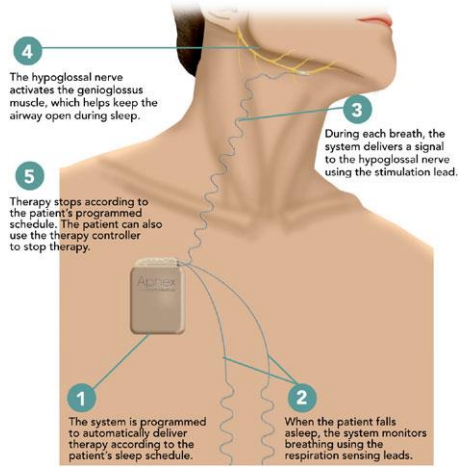
Lee A. Surkin, MD, FACC, FCCP, FASNC, FAASM
Founder, American Academy of Cardiovascular Sleep Medicine
President, Empire Sleep Medicine

Treatment Outcomes – CPAP or other…

- Improved quality of life
- Associated with better blood pressure control
- Decreases sympathetic activity
- Decreases recurrent Atrial Fibrillation
- Improves cardiac function
- Decreases early signs of Atherosclerosis
- Uncertain impact on long-term CAD (ADHERENCE IS KEY, Sleepy vs. Non-sleepy?, Male vs. Female?)
- Uncertain benefit in CHF patients

Alternative Treatment Options





Summary

- OSA is a validated CV risk factor
- OSA is independently associated with hypertension, arrhythmias, CHF, CVA, MI, CV death and all cause mortality
- High prevalence of OSA contributes to increased CV risk in population
- CPAP may result in decreased CV risk with adherence to therapy
- Longer term and additional trials are needed

NM: Vignette Patient

Get this person a Sleep Evaluation STAT!!!

Thank You!


American Academy of Cardiovascular Sleep Medicine
Lee A. Surkin, MD, FACC, FCCP, FASNC, Founder
ABIM Board Certified in Sleep Medicine
ABIM Board Certified in Cardiovascular Disease
drsurkin@aacsm.org
www.aacsm.org