بسم الله الرحمن الرحيم

Sleep Disordered Breathing: CV Implications

By

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Overview

- Definitions
- Types of sleep apnea
- Prevalence
- Current issues in sleep apnea
- Diagnosis
- Acute and chronic effects of sleep apnea
- CHF and sleep apnea
- Clinical management of sleep apnea; current and future treatment modalities
- Conclusions

Definitions

Definitions

Sleep-disordered breathing (SDB):

Repeated pauses in breathing during sleep, leading to sleep fragmentation and decreases in oxyhemoglobin saturation. Often used interchangeably with the term sleep apnea.

Young et al N Eng J Med, 1993

Definitions

Apnea:	Cessation of Airflow > 10 sec
Hyponea:	>50% reduction in airflow for >10 sec
AHI:	Apnea Hypopnea Index: the number of apneas and hypopneas per hour of sleep
Severity:	–Normal: AHI < 5 –Mild: AHI 5 – 15 –Moderate: AHI 15 – 30 –Severe: AHI >30
Sleep Apnea Syndrome (SAS)[3]:	AHI of $\geq$ 5 with symptoms.

American Academy of Sleep Medicine,1999

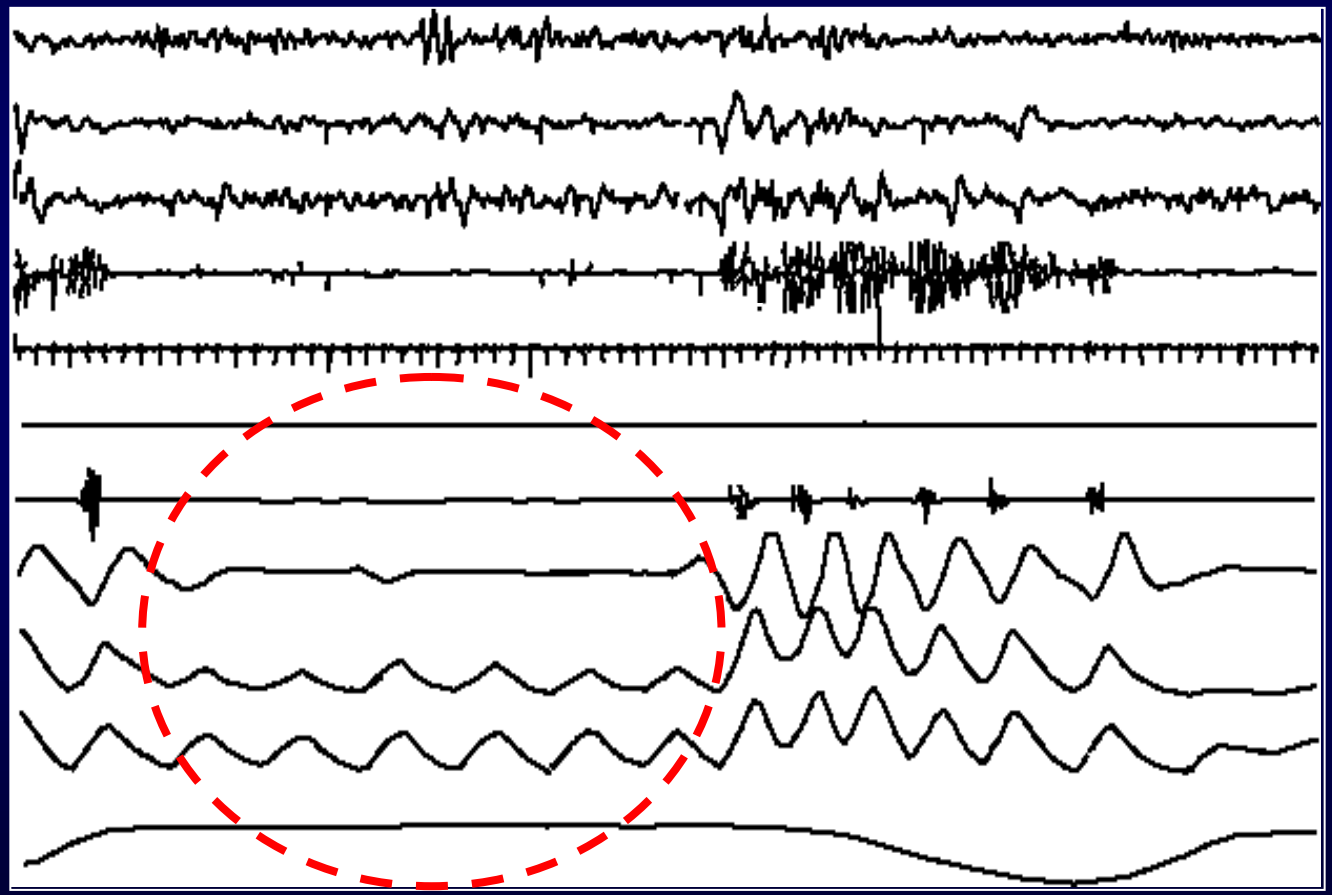
Types of Sleep Apnea

Types of Sleep Apnea

- ***Obstructive (OSA):***
  - Apnea with ventilatory efforts due to pharyngeal collapse
  - ~90% of sleep apnea cases
- ***Central (CSA):***
  - Apnea without ventilatory effort due to withdrawal of central drive
  - Thought to be due to decreased cardiac output
  - Cheyne-Stokes respiration a subset of CSA
  - ~10% of sleep apnea cases
- ***Mixed:***
  - Apnea with central component followed by obstructive component
  - Often classified as obstructive sleep apnea

Obstructive Apnea (Effort, No Flow)

EEG
EOG/L
EOG/R
EMG
EKG
LAT/RAT
SNORING
FLOW
Effort/Thorax
Effort/Abdn
SaO_2



Central Apnea (No Effort, No Flow)

EEG

EOG/L

EOG/R

EMG

EKG

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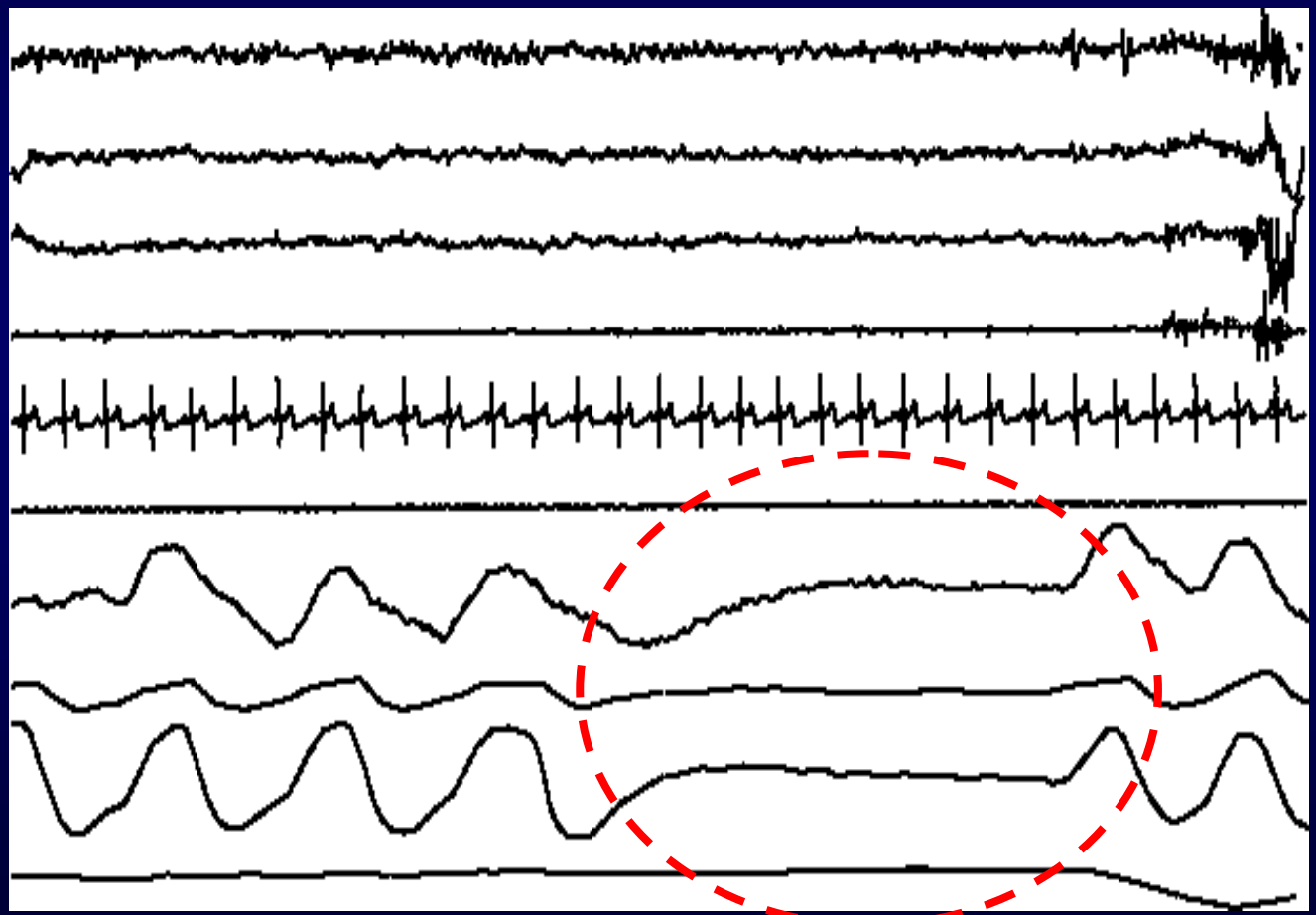
FLOW

Effort/Thorax

Effort/Abdn

SaO_2



Prevalence of Sleep Apnea

Prevalence of Sleep Apnea in the General Population

- **In individuals aged 30-60 years:**
  - **9% of women and 24% of men have AHI ≥ 5**
  - **2% of women and 4% of men have Sleep Apnea Syndrome**
    - **AHI ≥ 5 + symptoms of daytime sleepiness**
  - **4% of women and 9% of men have AHI≥15**
    - **Common threshold for treatment**
  - **>10% of individuals over the age of 65 years**
  - **Vast majority undiagnosed**

>12 million people in the U.S. alone

Prevalence of Obstructive Sleep Apnea in the General Population

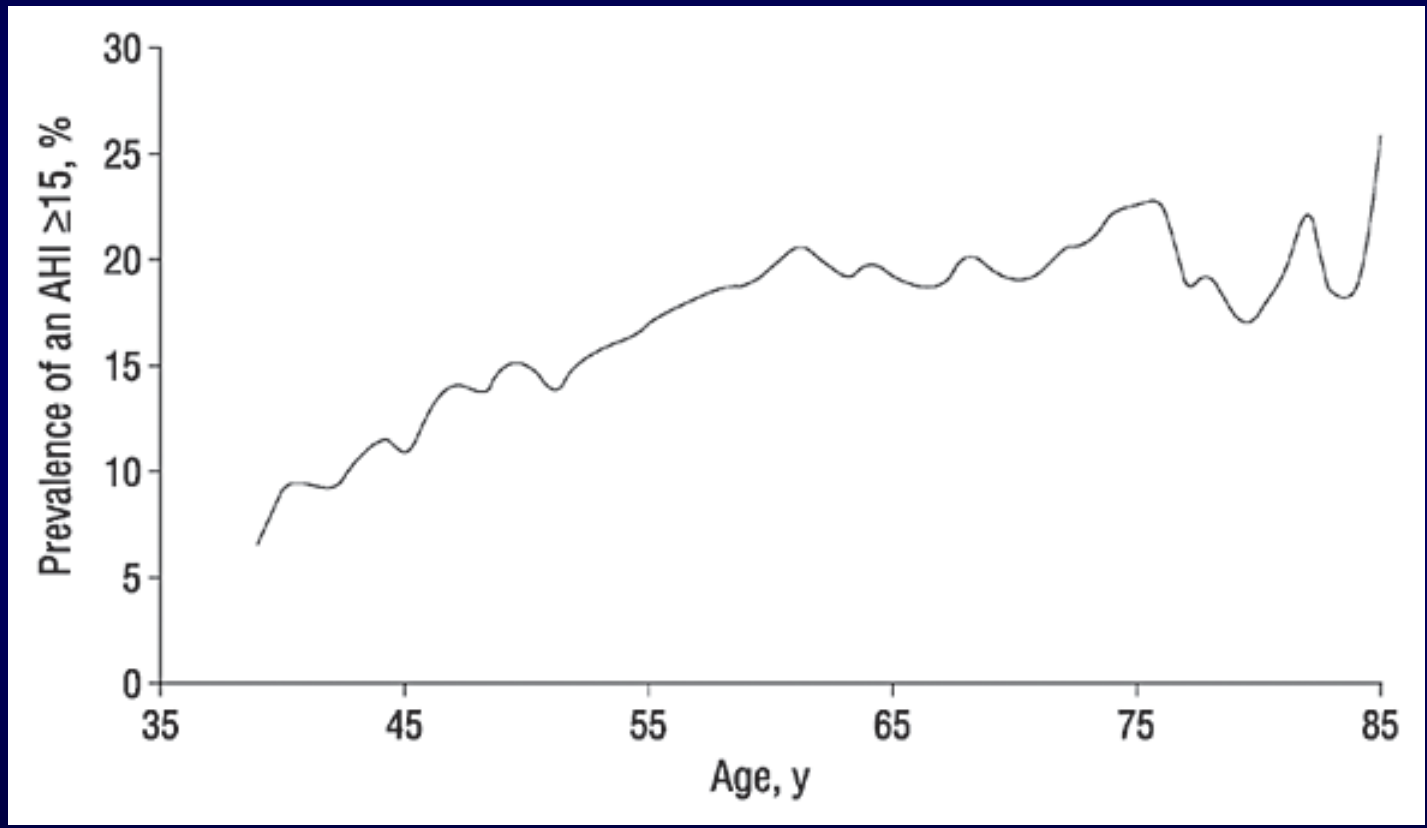
Prevalence of Obstructive Sleep Apnea From Three Studies with Similar Design and Methodology

			Estimated Prevalence of AHI ≥ 5 events/hour (% [95% CI])		Estimated Prevalence of AHI ≥ 15 events/hour* (% [95% CI])	
Study Location	**N**	**Age Range (years)**	**Men**	**Women**	**Men**	**Women**
Wisconsin[9]	602	30-60	**24** (19-28)	**9** (6-12)	**9** (6-11)	**4** (2-7)
Pennsylvania[10,11]	1,741	20-99	**17** (15-20)	Not given	**7** (6-9)	**2** (2-3)
Spain[12]	400	30-70	**26** (20-32)	**28** (20-35)	**14** (10-18)	**7** (3-11)

* Common threshold for treatment.

Young T, et al. Am J Respir Crit Care Med. Vol 165. pp 1217-1239, 2002.

Prevalence of Sleep Disordered Breathing in the General Population



Young T, et al. *Arch Intern Med* 2002; 162: 893-900.

Prevalence of Sleep Apnea in Patients with Comorbidities

- **~50% of patients with heart failure**
- **>60% of patients with LVEF ≤ 40% without any history of heart failure (AHI ≥15)**
- **>30% of patients with essential hypertension**
  - **Increasing AHI correlates with increase BP**
- **30-50% of patients with CAD**
- **>20% of Parkinson disease patients**
- **~30% of medically refractory epilepsy patients**

Current Issues

Current Issues in Sleep Apnea

- Vastly underdiagnosed
  - 82-93% of moderate to severe OSA not diagnosed
- Complex clinical pathways; multiple specialties test and treat
- Lack of clearly understood diagnostic approach
  - Variations in diagnostic criteria
  - Variations in testing approaches: sleep lab vs. ambulatory home testing
- While PSG is commonly viewed as the “gold standard” in SA diagnosis, limited access to sleep labs can significantly delay diagnosis
- Poor acceptance and compliance with current treatments

Diagnosis

Diagnosis of Sleep Disordered Breathing

- *"High risk" patient groups*
  - CHF
  - Patients with LVEF ≤ 40% without signs of heart failure
  - Premature Coronary Artery Disease
  - Refractory Hypertension
  - Stroke or TIA history
  - Patients with physical abnormalities in nose/throat
  - Patients who snore loudly and are overweight
  - Post-menopausal women
- *Screener questions and questionnaires*
  - Berlin questionnaire, Epworth Sleepiness Scale
  - Daytime fatigue; snoring and gasping; messy sleeper habits

Diagnosis of Sleep Disordered Breathing

- **Polysomnography (PSG):**

  Multichannel EEG, O2 sat, ECG, nasal airflow, rib cage movement, abdominal movement, ocular movement, limb movement

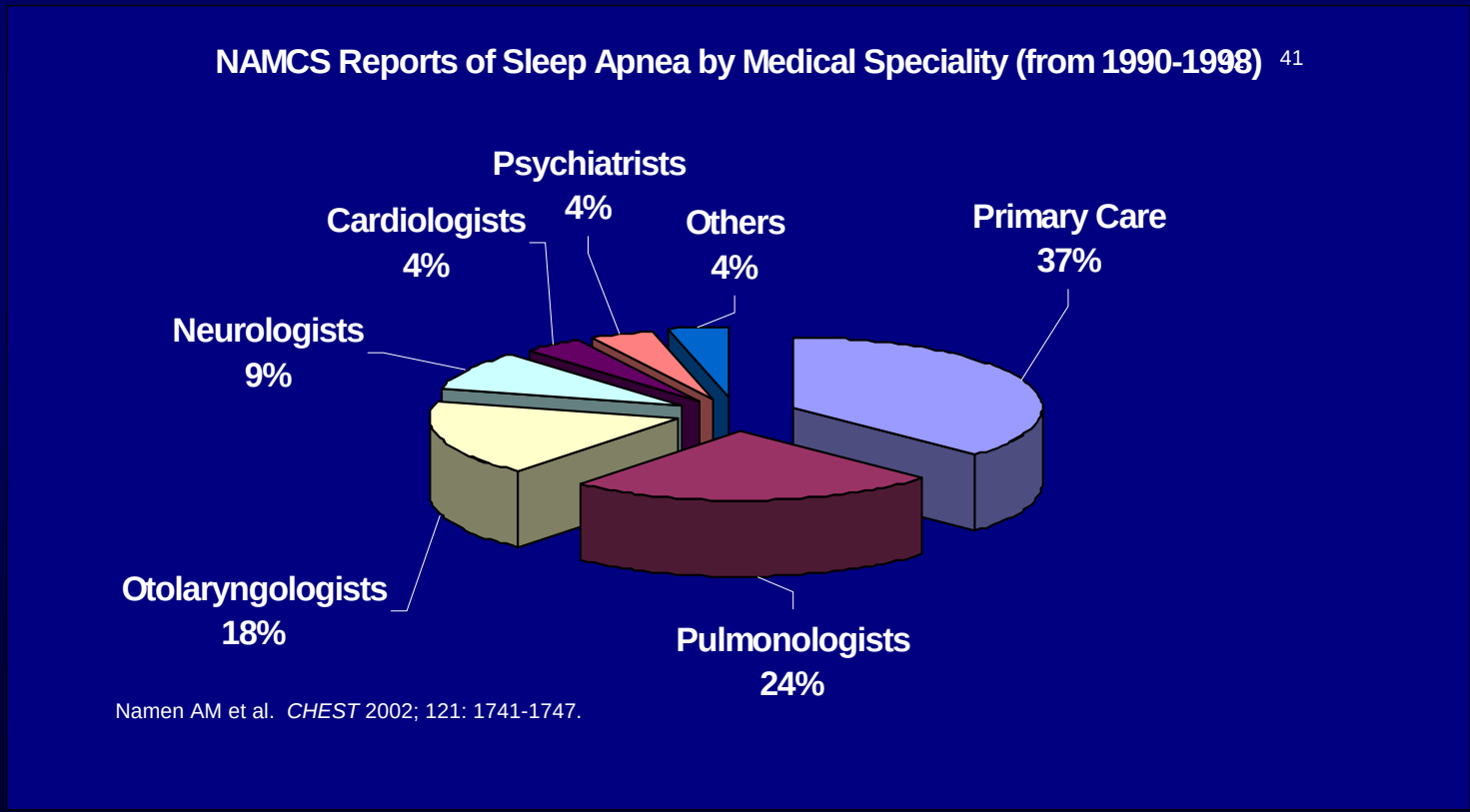
- **Output scored for:**
  - **Sleep latency**
  - **Sleep efficiency**
  - **Apneas and hypopneas**
  - **AHI - Apnea hyponea index**
  - **Arousals**
  - **Desaturations**

Diagnosis of Sleep Disordered Breathing

- ***Potential roll of ambulatory Polysomnography***
  - **Limited data channels**
  - **Limited reimbursement**
  - **Overcoming bottleneck in sleep lab**
- ***Role of the formal sleep study and sleep lab referral***
  - **Need for proper device and mask prescription**
  - **Need for appropriate patient follow-up to increase compliance**
  - **Issue of disease progression**

Implications for Cardiology

- **While Cardiologists account for only 4% of sleep apnea diagnoses, SA patients consume significantly more cardiovascular healthcare resources and are more likely to receive a comorbid diagnosis for cardiovascular disease in the five years prior to their sleep apnea diagnosis (Smith et al, Chest 2002)**



Acute and Chronic Effects

Acute Effects of Sleep Apnea

- ***Negative intrathoracic pressure***
  - **Increased LV transmural pressure**
  - **Increased afterload**
  - **Increased venous return**
  - **Diminished LV relaxation and filling**
  - **Reduced Stroke Volume and Cardiac Output**
  - **Vasoconstriction**
    - **Mediated through baroreceptor activation: Aortic and carotid**

Acute Effects of Sleep Apnea

- ***Hypoxia***
  - **Pulmonary artery vasoconstriction**
  - **Increased sympathetic nerve activity (SNA)**
  - **Surges in HR and BP at end of apnea**
  - **The degree of desaturation is directly related to increase in BP**
  - **O_2 administration has little effect**

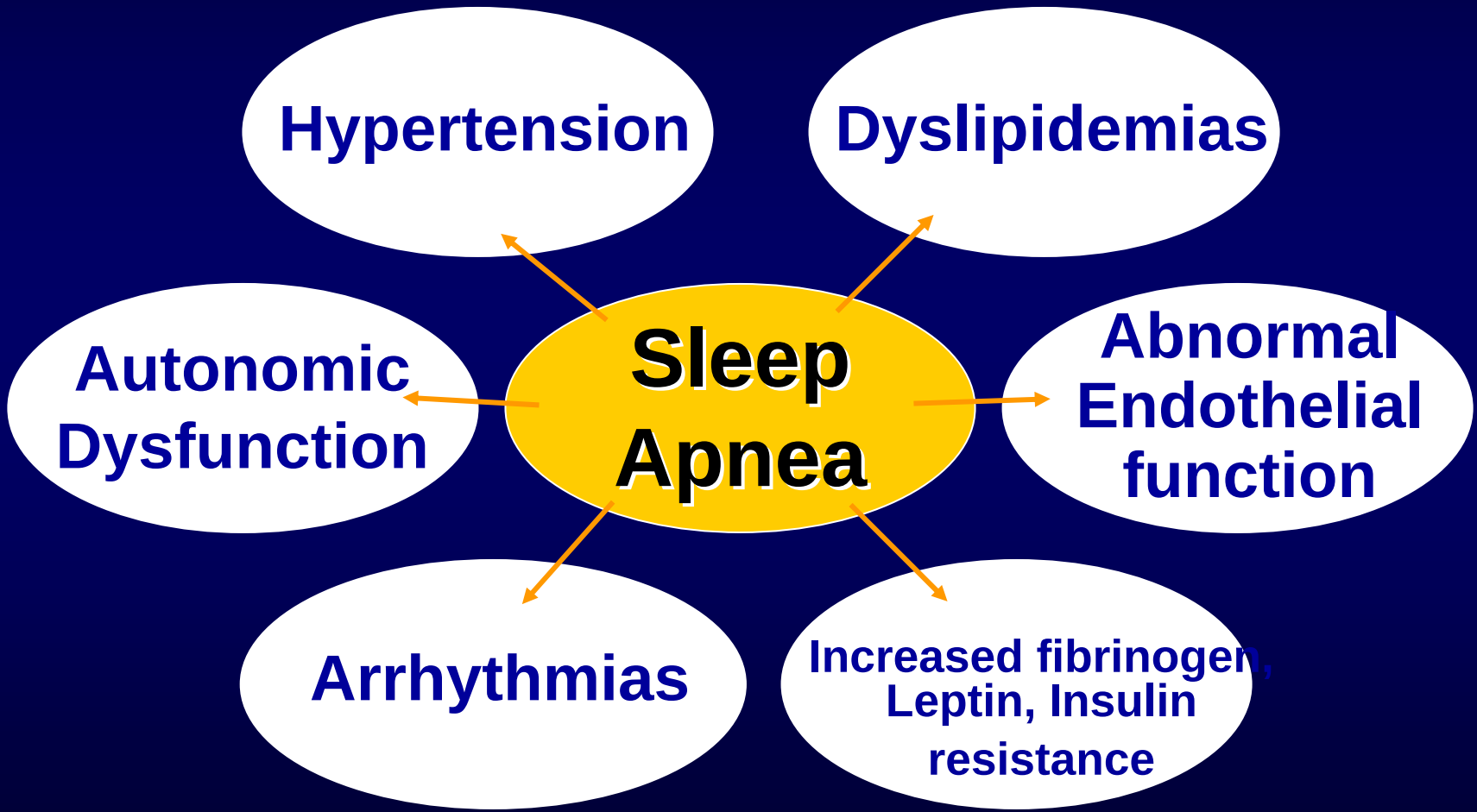
Chronic Effects of Sleep Apnea

- **Autonomic dysfunction**
  - Both sympathetic activation and parasympathetic withdrawal
  - Sleep and wake both effected
  - Increase in BP variability
  - Decrease in heart rate variability
  - Increased arrhythmia, V-Tach, Sudden Death
  - Hypoxia seems to exacerbate the dysfunction

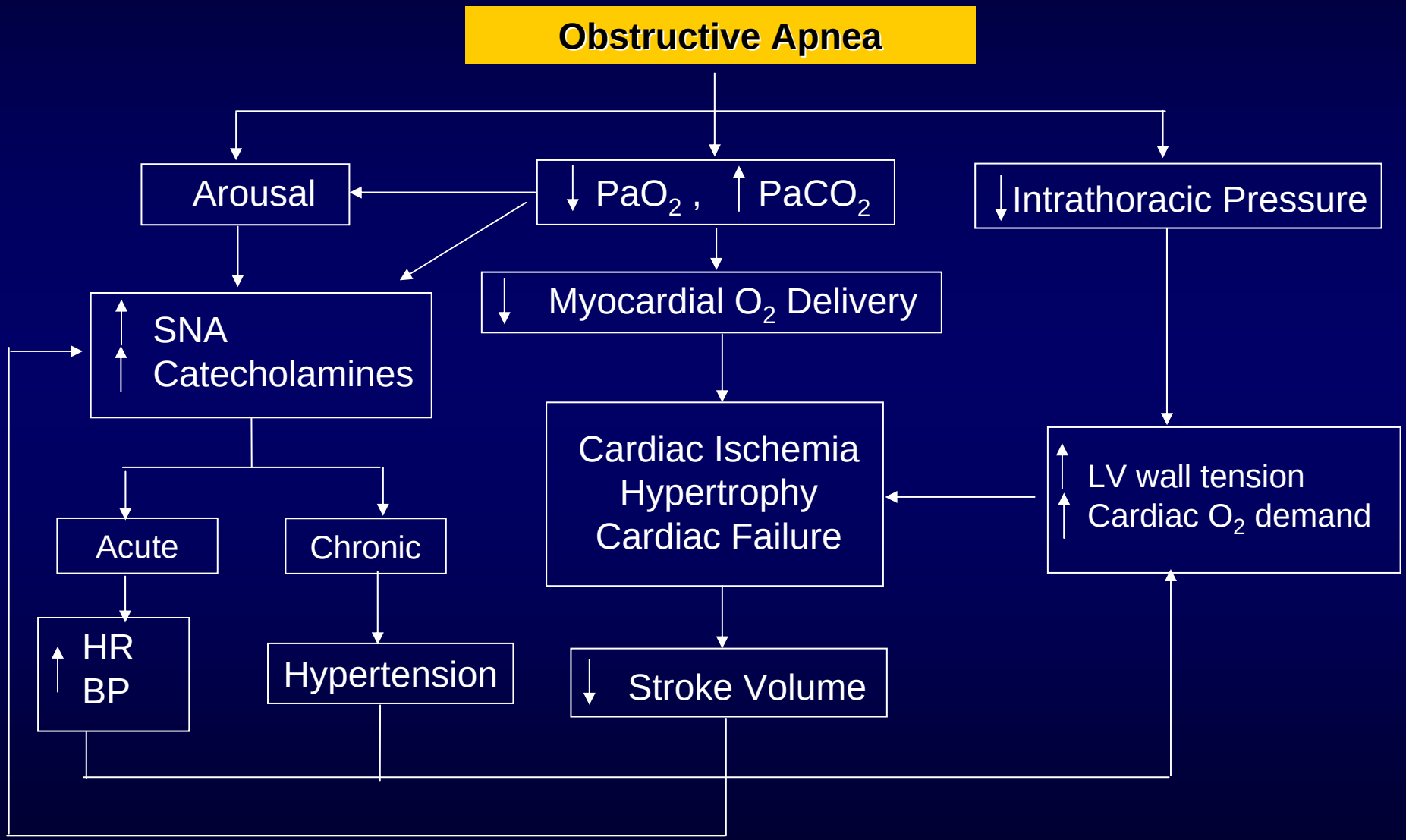
Chronic Effects of Sleep Apnea

- *Circulating hormones*
  - Atrial natriuretic peptide increased
  - Unclear results for renin, aldosterone, and vasopressin
  - Clear elevation in Endothelin-1 levels [53]
- *Insulin resistance*
- *Leptin resistance*
- *Increased PAI-1 and fibrinogen levels*
  - Role in atherosclerosis and thrombosis

Sleep Apnea and Cardiovascular Abnormalities



Effects of OSA on Cardiovascular System



Bradley, Floras, Journal of Cardiac Failure, 2:223-240

Cardiovascular Effects Sleep Heart Health Study

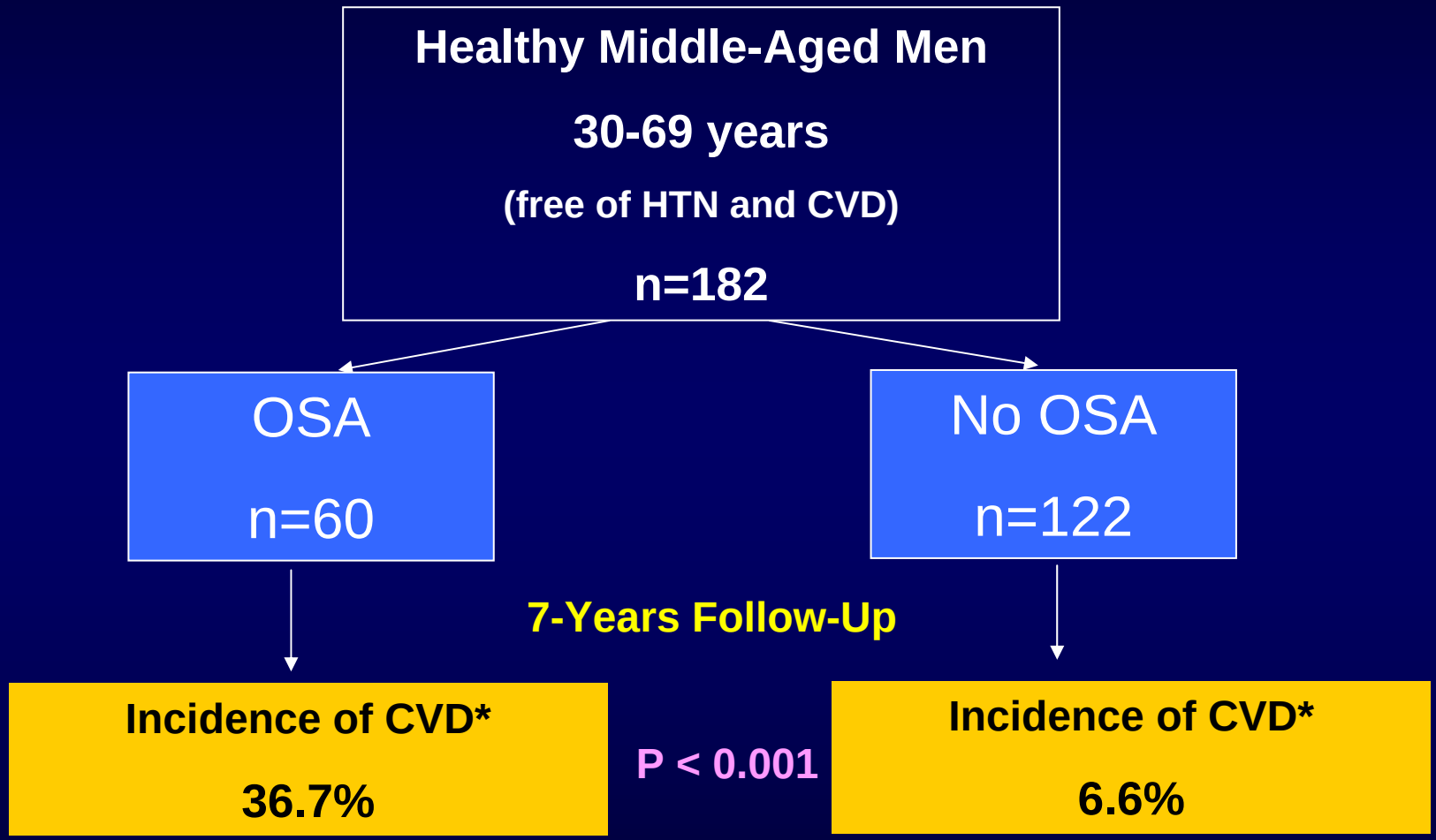
Patient Population:

- 6,424 individuals ≥ 40 years old screened for OSA
- Mean AHI 4.4 (minimal to mild OSA)
- 16% had history of CV disease or event: CHF, MI/ revascularization, stroke

Results:

- In patients with Apnea-Hypopnea Index ≥11:
  - Odds of CHF were 2.38x greater
  - Odds of ischemic disease were 1.27x greater
  - Odds of stroke were 1.58x greater

Cardiovascular Effects

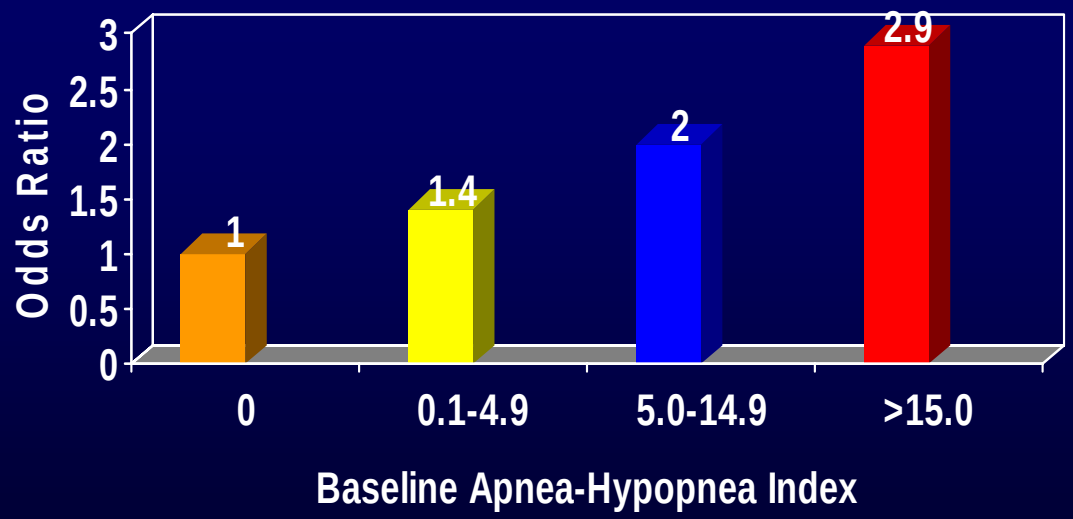


Peker Y, et al. Am J Respir Crit Care Med. Vol. 166. Pp 159-165, 2002.

Sleep Apnea and Hypertension

- ~30% of patients with hypertension have sleep apnea
- >60% of sleep apnea patients have hypertension

Odds Ratios for Hypertension at a Follow-Up Sleep Study, According to the Apnea-Hypopnea Index at Base Line*

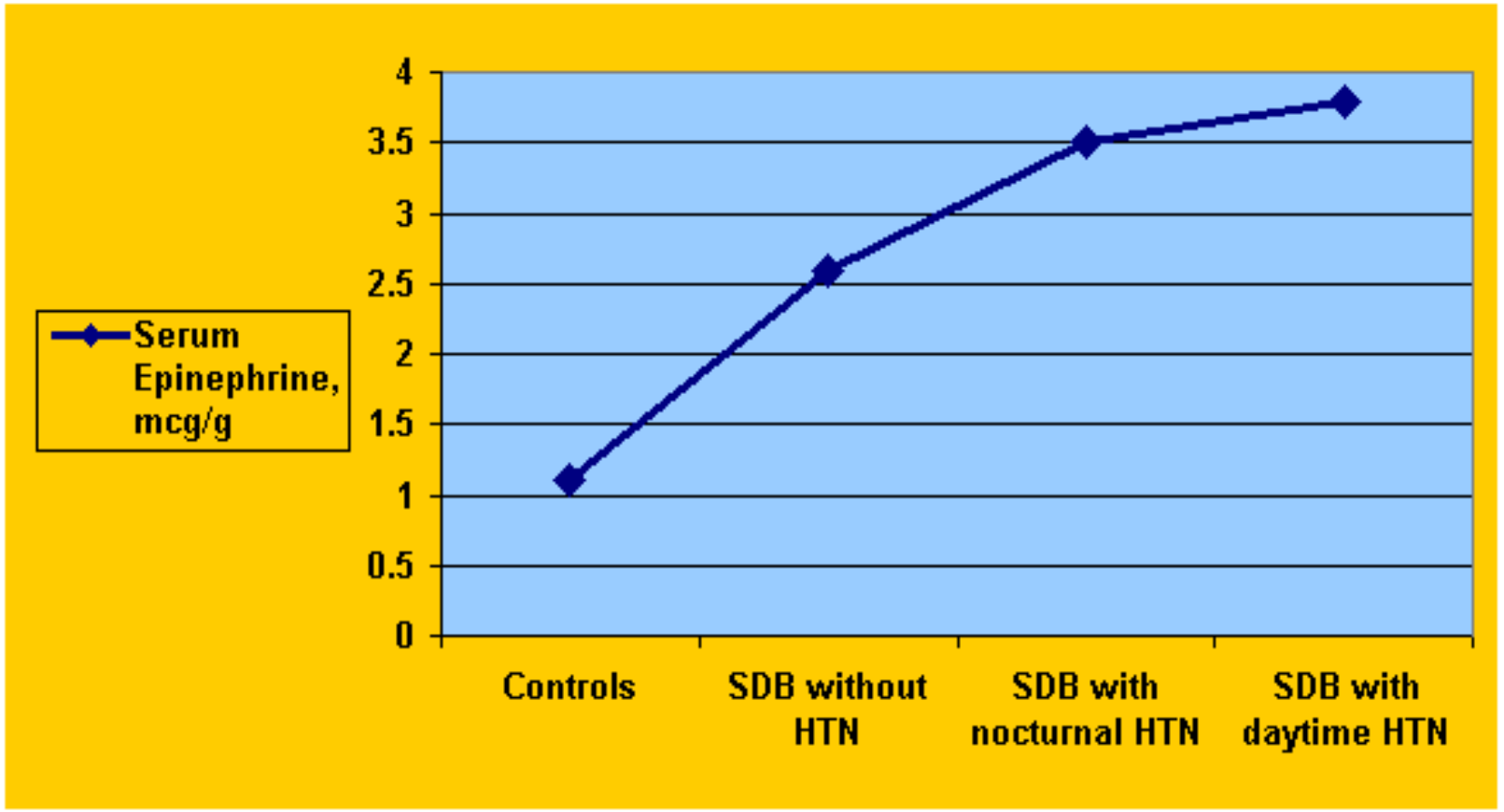


*Hypertension was defined as a BP ≥ 140/90 mmHg or the use of antihypertensive medications.

Data extracted from Table 3: Peppard P et al. N Engl J Med 2000; 342: 1378-84.

Role of SNS SDB & HTN Association

Figure 1. Serum Epinephrine Levels in SDB Patients Vs Controls

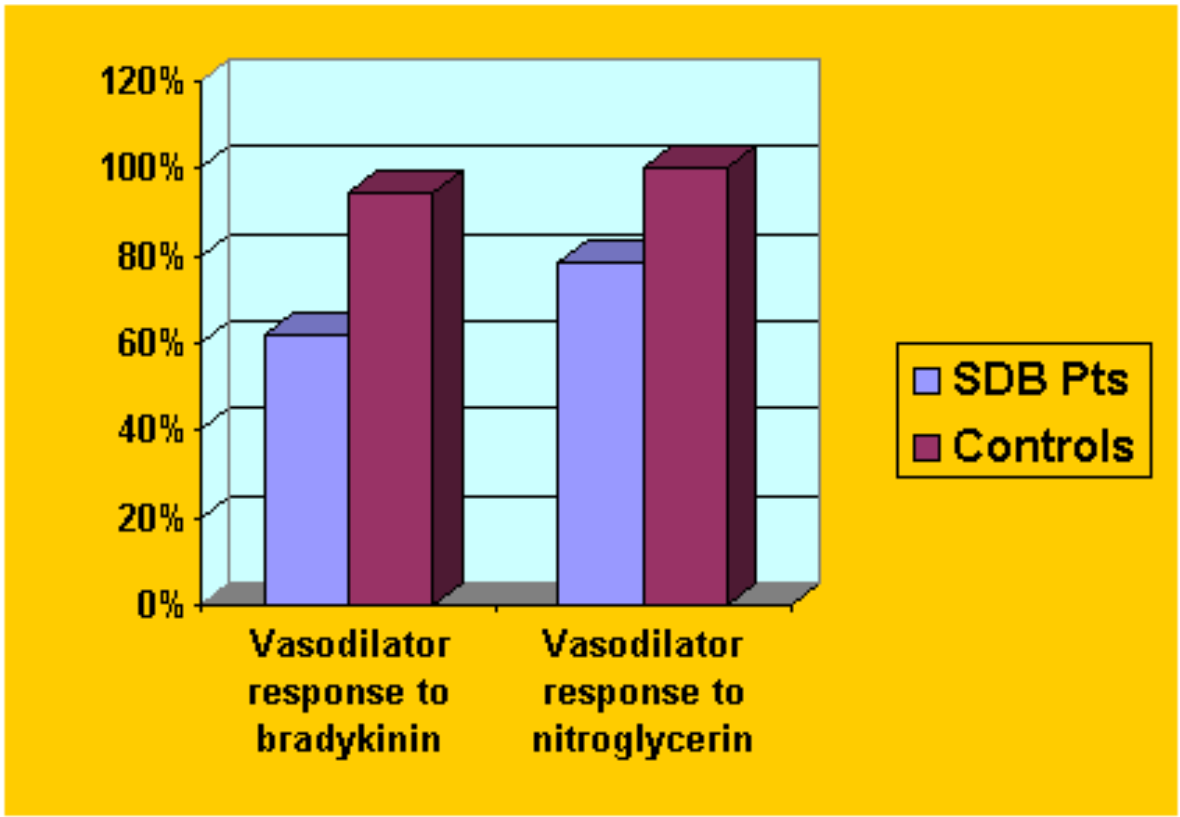


From Garcio-Rio F, et al, Chest 2000;117:1417-1425

Vascular Reactivity in SDB

Figure 2

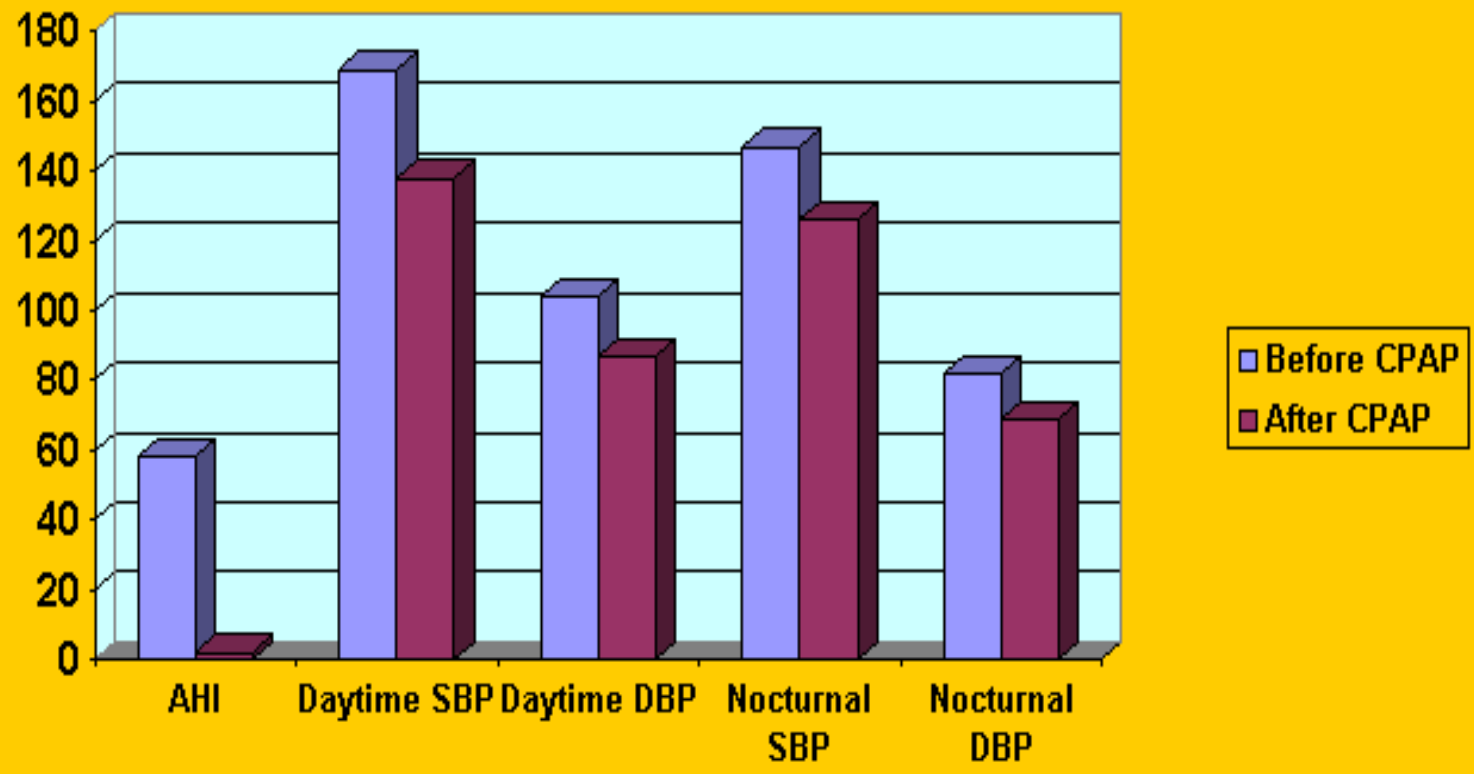
Vasodilator Response to Bradykinin in SDB Patients Vs Controls



From Duchna HW, et al, Am J Resp Crit Care Med 2000;161:187-91

Effect of Treatment of SDB on BP

Figure 3. Effect of CPAP on Blood Pressure in SDB Patients After 6 Months



From Mayer J et al. Cardiology 1991;79:84-92

SDB & HTN Summary

- A substantial proportion of patients with HTN will have underlying SDB
- The link between SDB & HTN is difficult to establish due to confounding variables as obesity age and sex
- HTN is associated with all grades of SDB and risk of HTN is dose dependent to the degree of SDB
- SDB is associated with increased SNS activity both during sleep and arousal

SDB & HTN Summary

- **SDB is associated with abnormal vascular reactivity and BP Non-dipper**
- **Treatment of SDB with CPAP is associated with control of HTN**
- **Though B-Blockers have a theoretical benefit, no single antihypertensive class has a specific benefit in treatment of SDB associated HTN**

Sleep Apnea and Coronary Artery Disease

- 30-50% of patients with CAD have sleep apnea
- OSA is an associated with an increased risk of cardiovascular mortality in patients with CAD

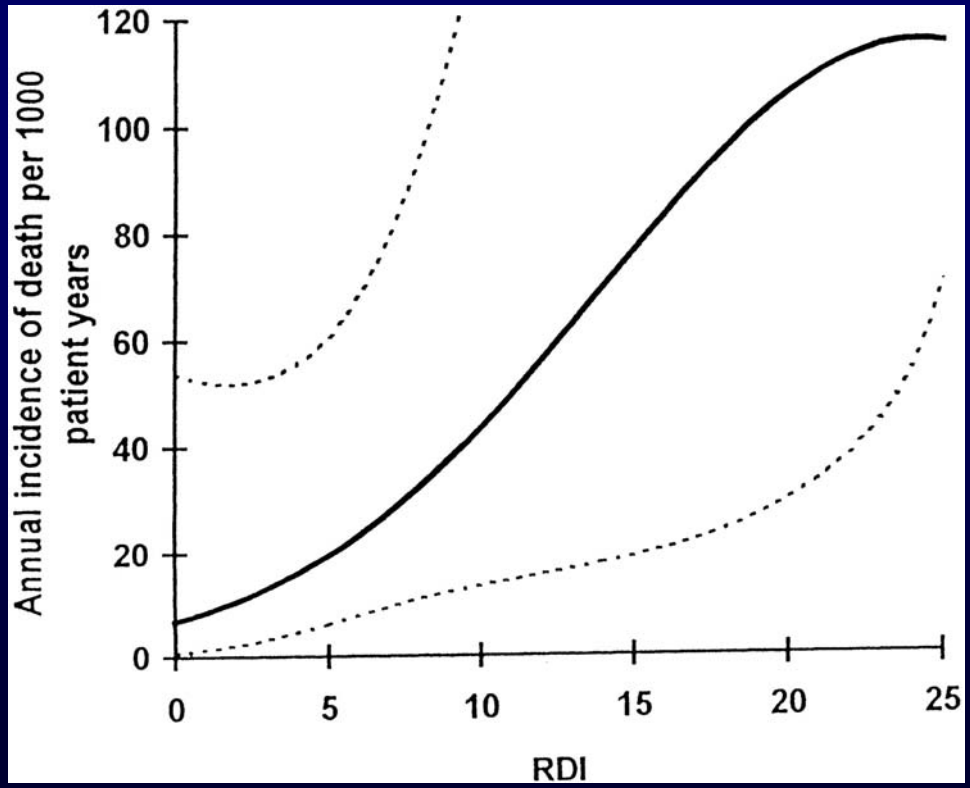


Figure 1. **By use of a Poisson model the death hazard was calculated as a function of RDI, current age, and time elapsed after the intensive care episode for CAD. The *bolded curve* gives the function at the current age 70 yr and 3 yr after intensive care. The *dotted curves* represent 95% CI. Peker Y, Hedner J, Kraiczi H, et al. Am J Respir Crit Care Med. Vol. 162. Pp 81-86.**

Sleep Apnea and Cardiac Arrhythmias

- ***Bradyarrhythmias:***
  - **AV Block and asystoles have been reported in up to 10% of patients with sleep apnea**
- ***Tachyarrhythmias and ventricular ectopy:***
  - **Ventricular ectopy has been reported in up to 66% of patients with sleep apnea syndrome**
  - **Ventricular tachycardia more common in patients with sleep apnea (0-15%) vs. the general population (0-4%)**

Sleep Apnea and Cardiac Arrhythmias

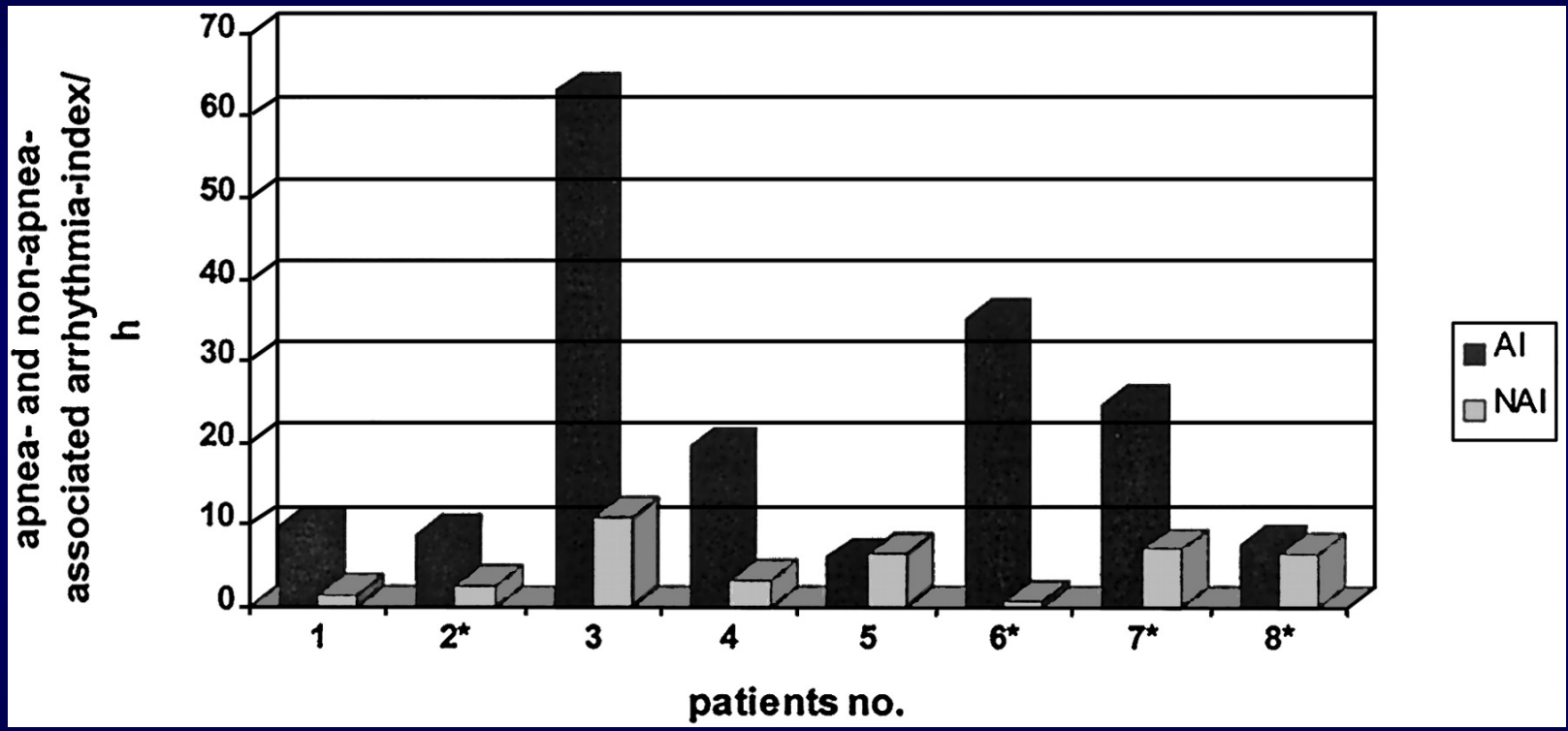
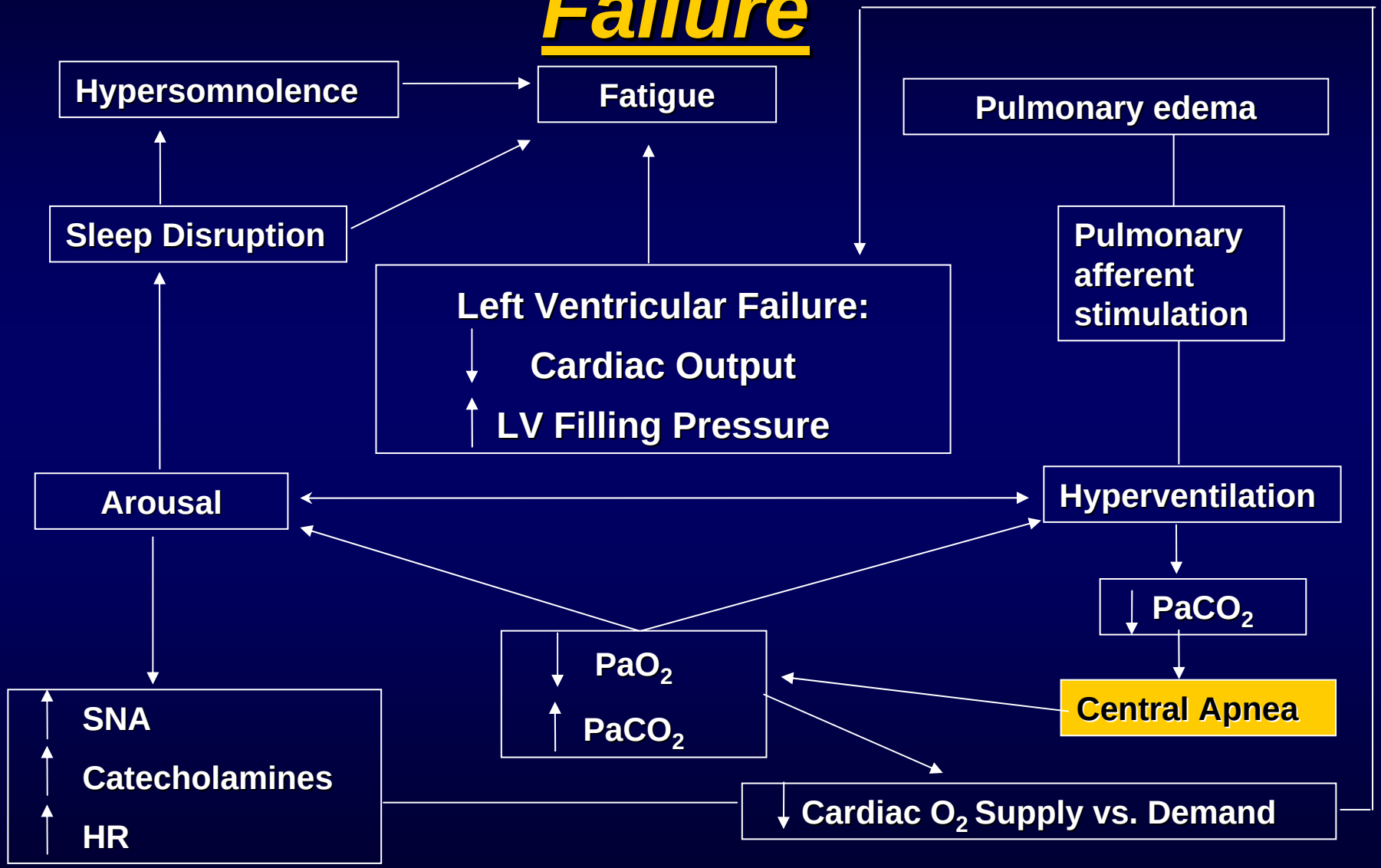


Figure 1. Comparison of the number of ventricular arrhythmias occurring simultaneous to disordered breathing (AI) and ventricular arrhythmias occurring during the time of normal breathing (NAI) in all patients with sleep-related breathing disorders and ventricular tachyarrhythmias during sleep. *Indicates patients with CSR. Fichter J, et al. *Chest.* 2002;122:558-561.

Central Sleep Apnea and Heart Failure



Bradley, Floras, Journal of Cardiac Failure, 2:223-240

Sleep Apnea and CHF

- Prevalence of CHF is 4.9 MM Americans
- ~50% of patients with heart failure have sleep apnea
- >60% of patients with LVEF ≤ 40% without any history of heart failure (AHI ≥15) have sleep apnea
- High co-morbid incidence of SDB
  - End stage CHF – Cheyne Stokes Respirations
  - Obstructive SAS probably grossly under recognized
  - Vascular reactivity abnormalities
  - Renal perfusion and sodium retention

Sleep Apnea and CHF

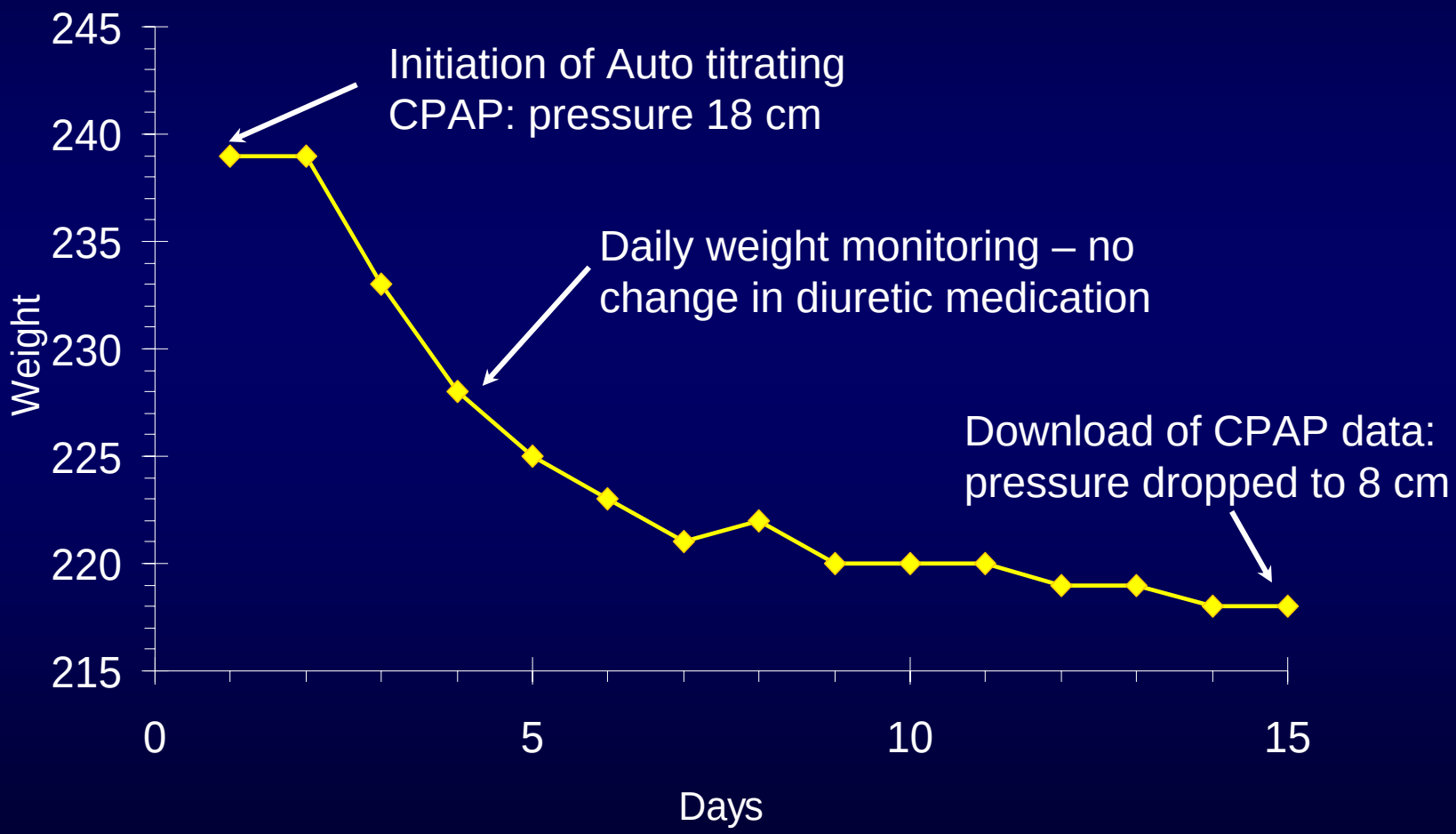
- Most CHF exacerbations due to volume overload
  - Dietary and medication compliance issues
  - Lack of adequate monitoring or recognition of weight gain
- Potential interaction of SDB and CHF include:
  - Activation of Sympathetic nervous system
  - Vascular reactivity abnormalities
  - Renal perfusion and sodium retention

Bradley, Floras, Journal of Cardiac Failure, 2:223-240

Case Presentation

- 78y/o WM
- CABG 1996
- 2000 – totals car in auto accident
- Hospitalized for “new onset CHF”
- Diuresis results in renal failure
- Hemodialysis initiated
- Sleep apnea dx
- Creatinine returns to baseline (1.3-1.5) following initiation of CPAP 10cm H_20
- 18 months later:
  - 30# weight gain
  - Snoring louder
  - More fatigued
  - Remains off dialysis

Effect on CHF volume overload



Sleep Apnea and CHF: Clinical Observations

1. Patients with OSA and CHF may be prone to volume related changes in upper airway resistance.
2. Changes in effectiveness of CPAP may diminish renal perfusion and augment unwanted sodium and fluid retention.

Sleep Apnea and CHF: Clinical Observations

3. Patients with OSA and volume overload do not respond as well to oral diuretics and may have worsening renal function.
4. Documenting and treating increases in airway resistance have important and dramatic clinical effects on CHF.
5. Effectively treating OSA can have a positive impact on HF status.

Clinical Management of Sleep Apnea: Current and Future Treatment Options

Clinical Management Methods

- ***Current:***
  - **Nonsurgical treatment:**
    - **Behavior modifications**
    - **Nasal Continuous Positive Airway Pressure (CPAP)**
    - **Oral appliances**
  - **Surgical treatment:**
    - **Nasal surgery**
    - **Uvulopalatopharyngoplasty**
    - **Laser-assisted uvulopalatoplasty**
- ***Future:***
  - **Pacemakers?**

Behavioral Modifications

Methods:

- Weight loss
- Avoidance of alcohol, sedatives, antihistamines, smoking
- Sleeping on side vs. back

Pros:

- Lower risk (vs. surgical/invasive methods)
- Easier to implement and lower cost
- Even a moderate weight loss of 10% corresponds to ~30% decrease in AHI

Cons:

- Only effective in mild to moderate SDB
- Requires active patient participation
- Patient compliance low

Continuous Positive Airway Pressure

Methods:

- Pneumatic stent to keep upper airway open
- CPAP vs. BiPAP vs. Variable pressure (AutoPAP)

Pros:

- Non-invasive
- Demonstrated to improve AHI, SA symptoms, hypertension, and heart failure status with effective use
- Effective in 80-90% of patients (when used appropriately) and can be used in infants, children, and adults

Cons:

- Patient compliance low (short term compliance ~50%)
  - Intensive support and customization improves compliance

Oral Appliances

- ***Methods:***
  - Mandibular and tongue advancement to modify the upper airway and alleviate obstruction.
- ***Pros:***
  - Non invasive
  - Can be customized to patient
  - Effectiveness of ~40% reduction in baseline AHI
- ***Cons:***
  - ASDA recommended only with non-obstructive snoring or mild-to moderate sleep apnea
  - Long-term compliance <60%
  - Excessive salivation and temporomandibular joint discomfort are major complaints
  - May cause dental and skeletal changes

Surgical Treatment

Methods:

- Surgery to augment the upper airway and relieve obstruction:

  Uvulopalatopharyngoplasty (UPPP); Laser-assisted uvulopalatoplasty (LAUP); Tonsillectomy; Partial resection or ablation of the tongue; Major reconstruction of the mandible or maxillae; Tracheostomy; Nasal surgery

Pros:

- Surgical event—does not require ongoing patient compliance

Cons:

- UVPPP: 50% AHI reduction in 50% of patients
- LAUP: 30% of patients with mild to moderate OSA improve; 30% do not improve; 30% get worse
- Invasive procedures; surgical risk and painful recovery
- Expensive
- Irreversible

Potential Role(s) for Pacemakers*

- Pacers as sleep apnea detection devices
  - Respiratory detection
    - Balaban K, et al., Feasibility of Screening for Sleep Apnea Using Pacemaker Impedance Sensor. *PACE* 2001;24(4 Part II):617 (abstract)
    - Defaye P, et al., Feasibility of Sleep Apnea Detection Using a Pacemaker Minute-Ventilation Sensor. *PACE* 2002;25(4 Part II):546 (abstract)
  - Sleep apnea related heart rate changes
    - Guilleminault C, et al. Cyclical Variation of Heart Rate in Sleep Apnea Syndrome. *Lancet* 1984 Jan 21;1(8369):126-131

*In the United States pacemakers are currently not approved for sleep apnea indications.

Studies Using Pacing*

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- Garrigue S., et al., Night Atrial Overdrive with DDD Pacing Results in a Significant Reduction of Sleep Apnea Episodes and QOL Improvement in Heart Failure Patients. *PACE* 2001;24(4):575 (abstract).
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***In the United States pacemakers are currently not approved for sleep apnea indications.**

Overall Conclusions

- **Sleep-disordered breathing (sleep apnea) is a highly prevalent, underdiagnosed disease with significant effects on the cardiovascular system.**

- **Cardiologists can assist in the diagnosis of sleep apnea patients when the patient is being seen for other cardiovascular comorbidities.**

Overall Conclusions

- **Novel technology may improve efficacy and patient acceptance and provide the Cardiologist with more treatment options for SA patients.**

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Thank You