

PVDOMICS Sleep Core

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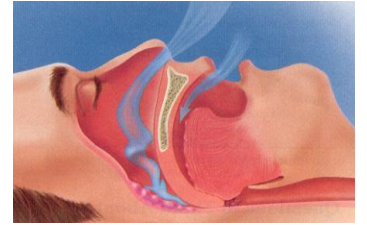


NHLBI Pulmonary Vascular Disease Phenomics Program

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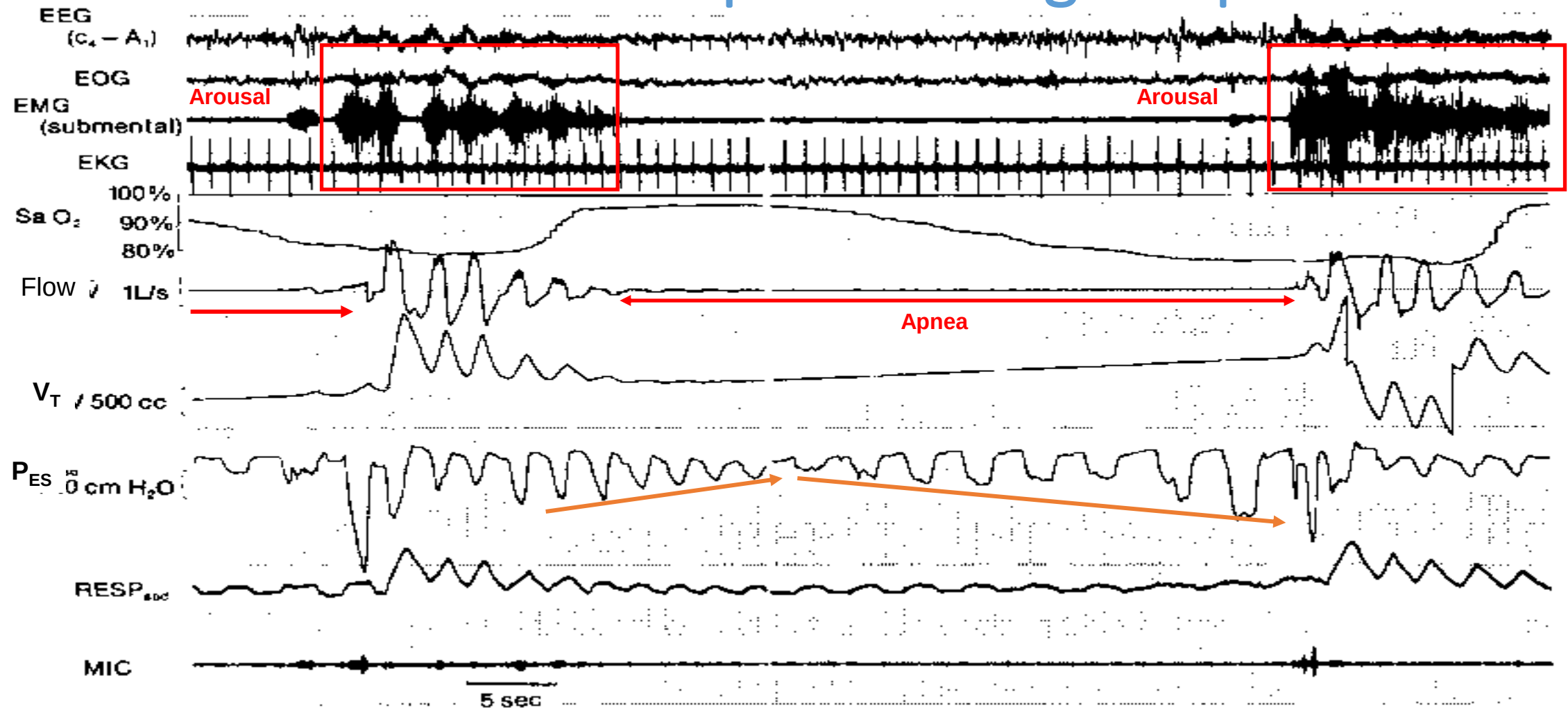
Obstructive Sleep Apnea

A Highly Prevalent, Under-recognized Physiologic Stressor



- **17% of the general adult population, increasing with obesity epidemic**
 - Nearly 1 in 15 affected by at least moderate sleep apnea
 - Young et al NEJM 1993, Peppard et al. Am J Epi 2013
 - **85% of cases estimated to be undiagnosed!**
 - Kapur VK et al Sleep and Breath 2002
- **30-40% of patients with CAD**
 - Moee T et al Chest 1996; Schaker et al H Cardiol 1999; Leung RS et al AJRCCM 2001
- **> 50% of patients with diabetes or hypertension or heart failure**

Recording of Obstructive Apnea During Sleep

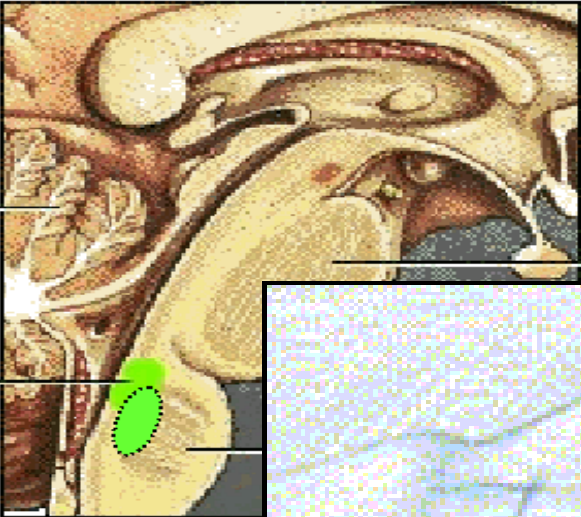


CENTRAL CHEMORECEPTORS

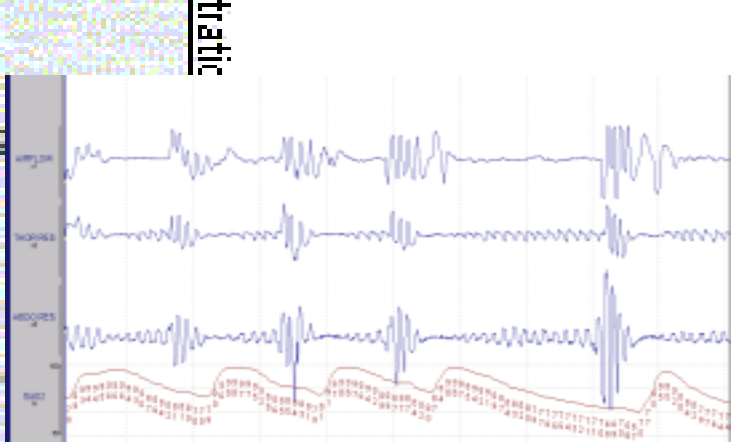
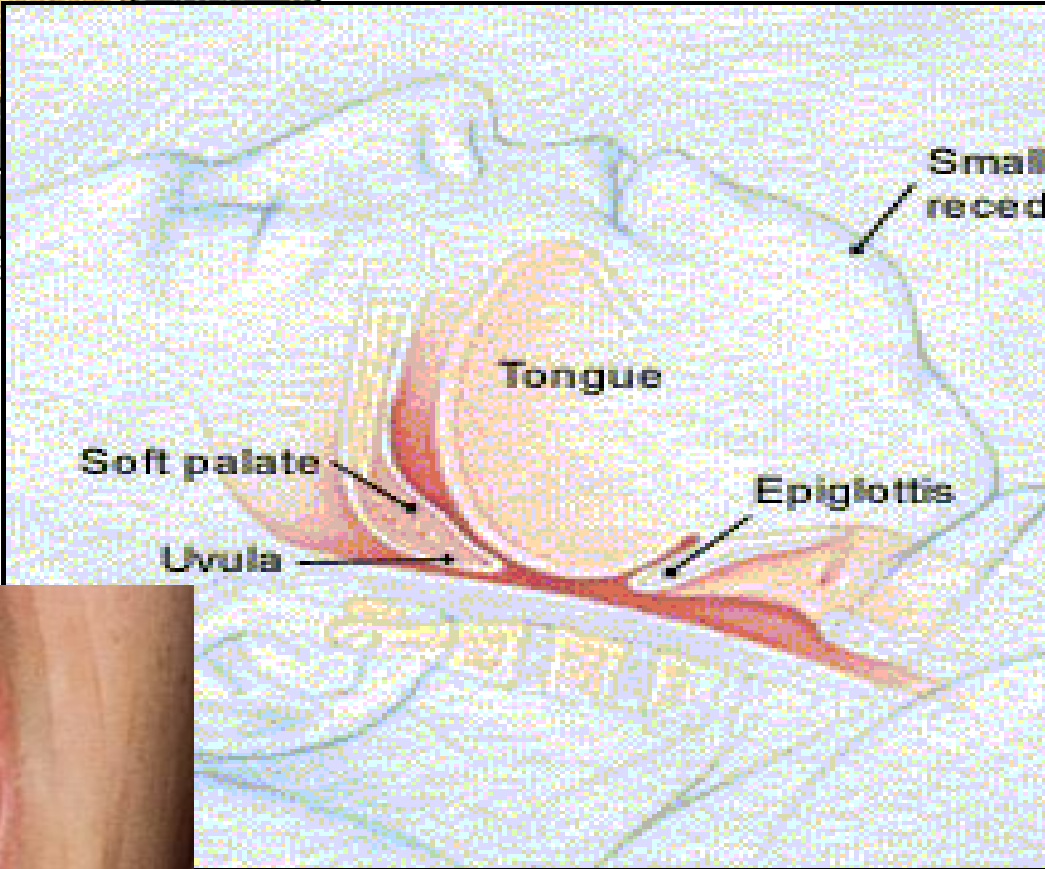
Cerebellum

Central chemoreceptors

Monitor the acidity and carbon dioxide



Pons



Sleep Apnea Severity Grading

	AHI	SaO₂ (%)	EKG
Mild	5 - <15	>85	Mild tachybradycardia
Moderate	15 - <30	75-85	Prominent tachybradycardia, Asystole <3 sec
Severe	≥30	<75	Asystole >3 sec, VT

Apnea-hypopnea index (AHI) - primary grading parameter

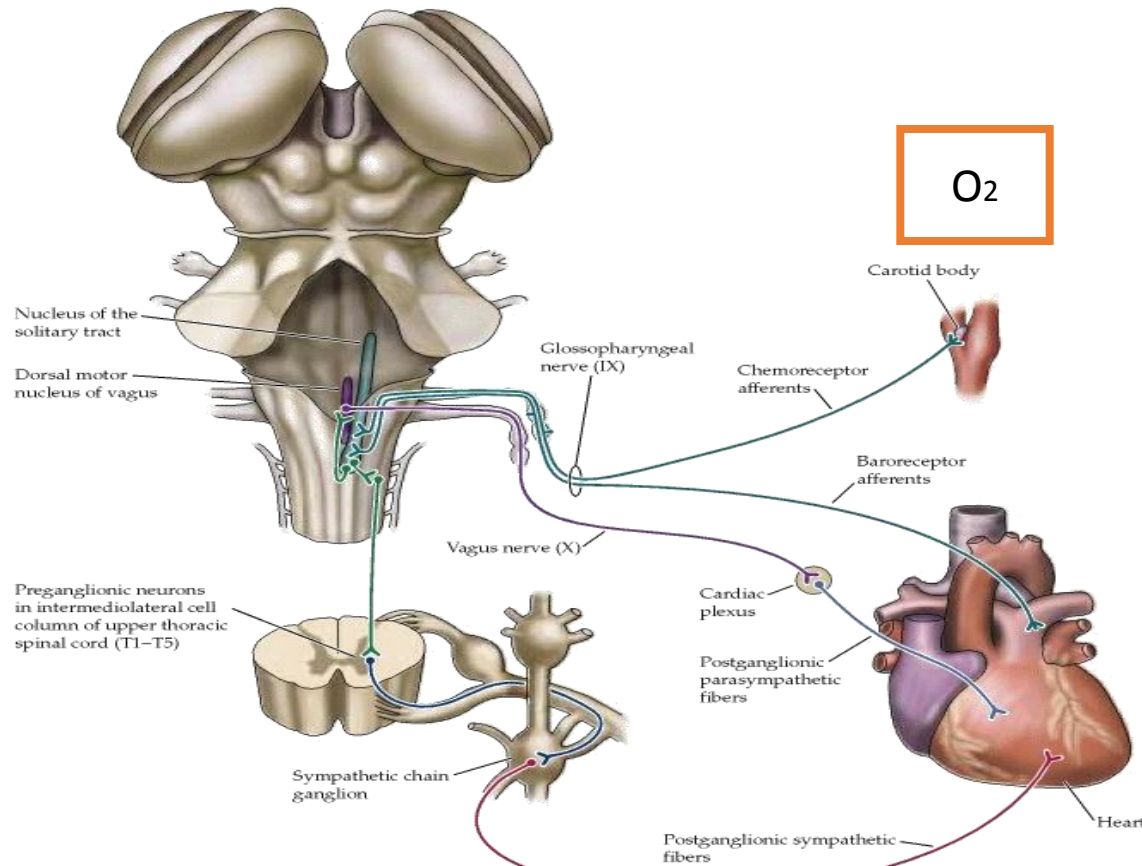
$$\text{AHI} = \frac{\text{apneas} + \text{hypopneas}}{\text{total sleep time (hr)}}$$

Central Sleep Apnea/Periodic Breathing

CO₂

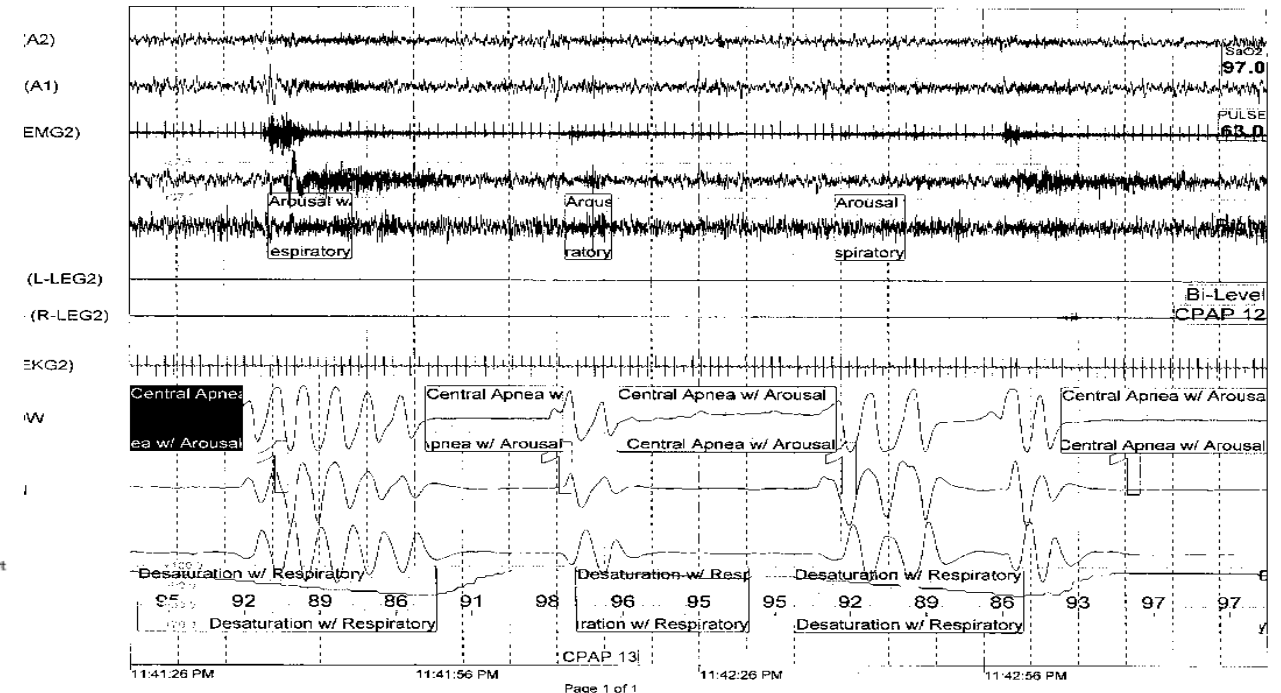
Pre-boetzing complex: Inspiration
Parafacial respiratory group: Expiration

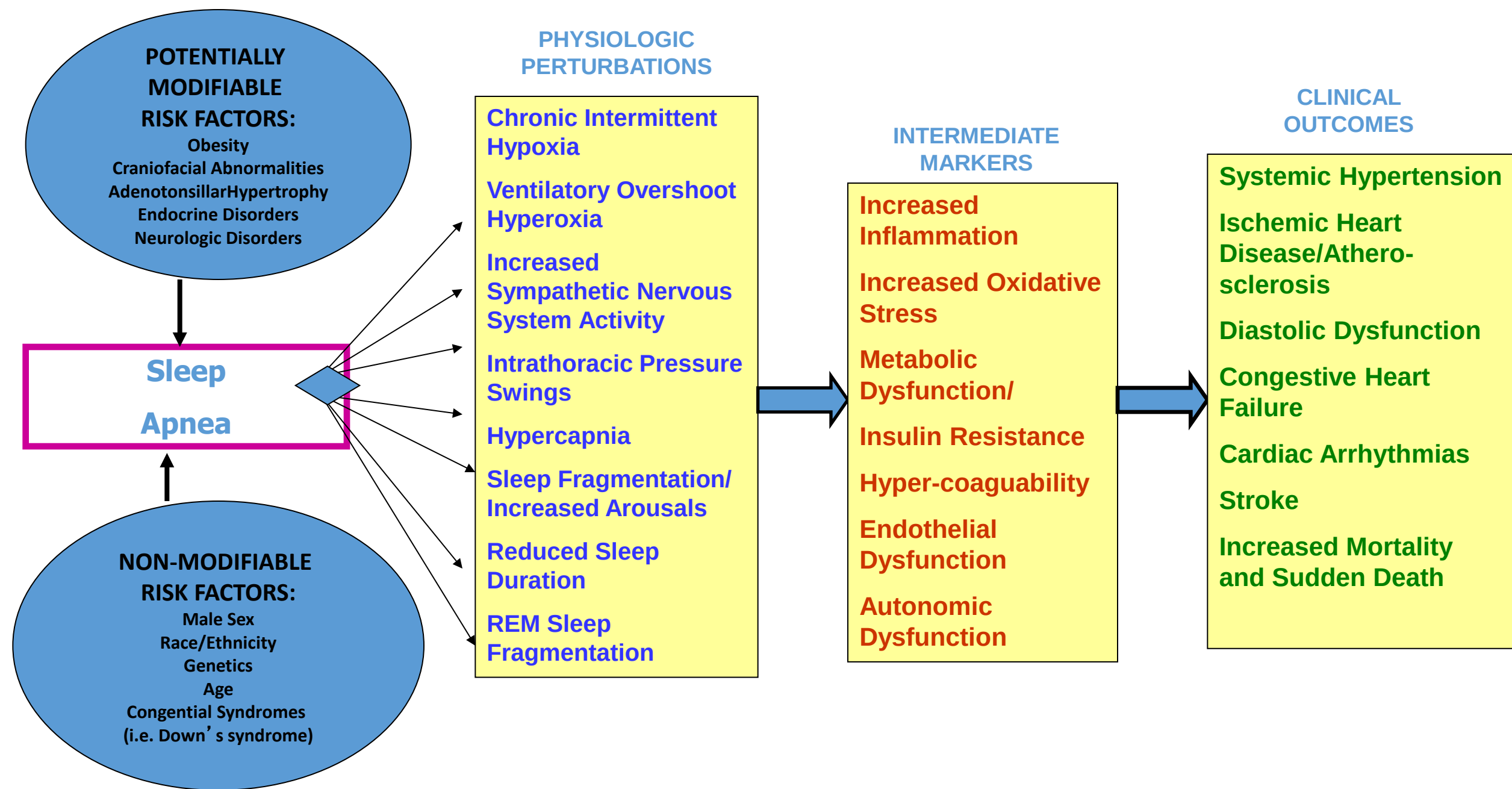
O₂



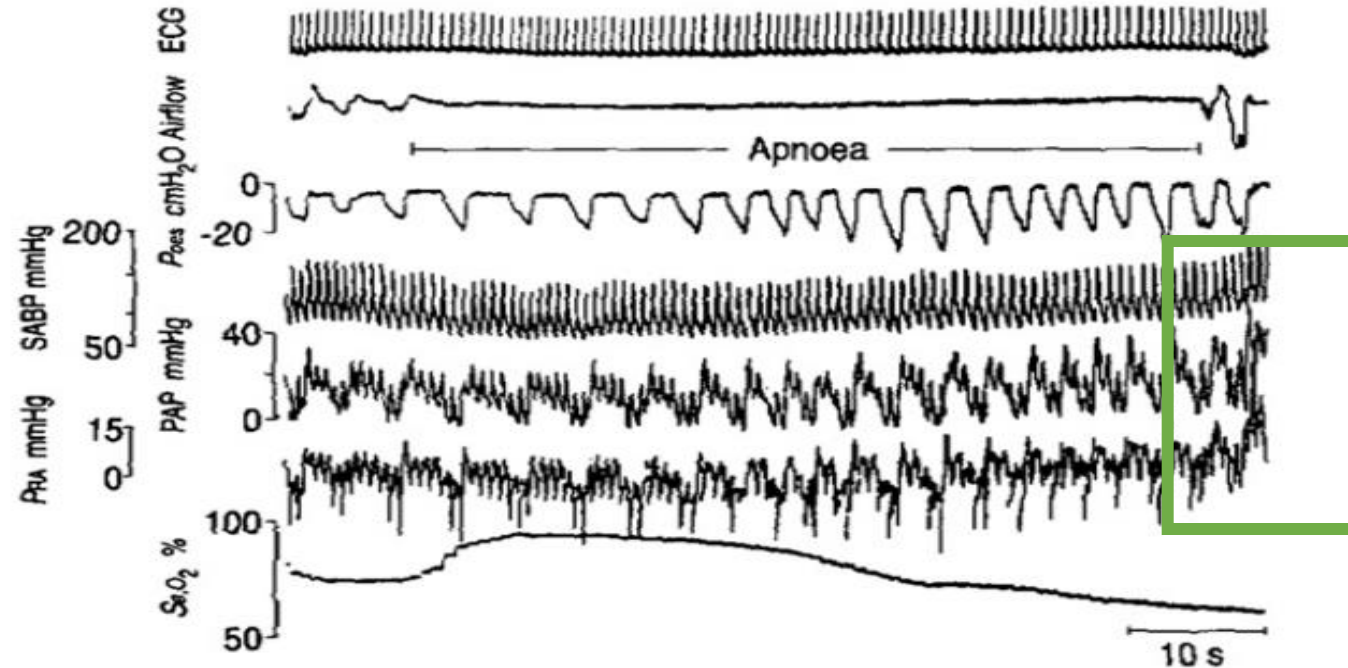
Breathing Instability

- Central apnea is a temporary failure of the generation of breathing rhythm
- Occurs when level of paCO_2 falls below the *apneic threshold*, a paCO_2 level below which breathing ceases
- Leads to lack of drive to breathe during sleep



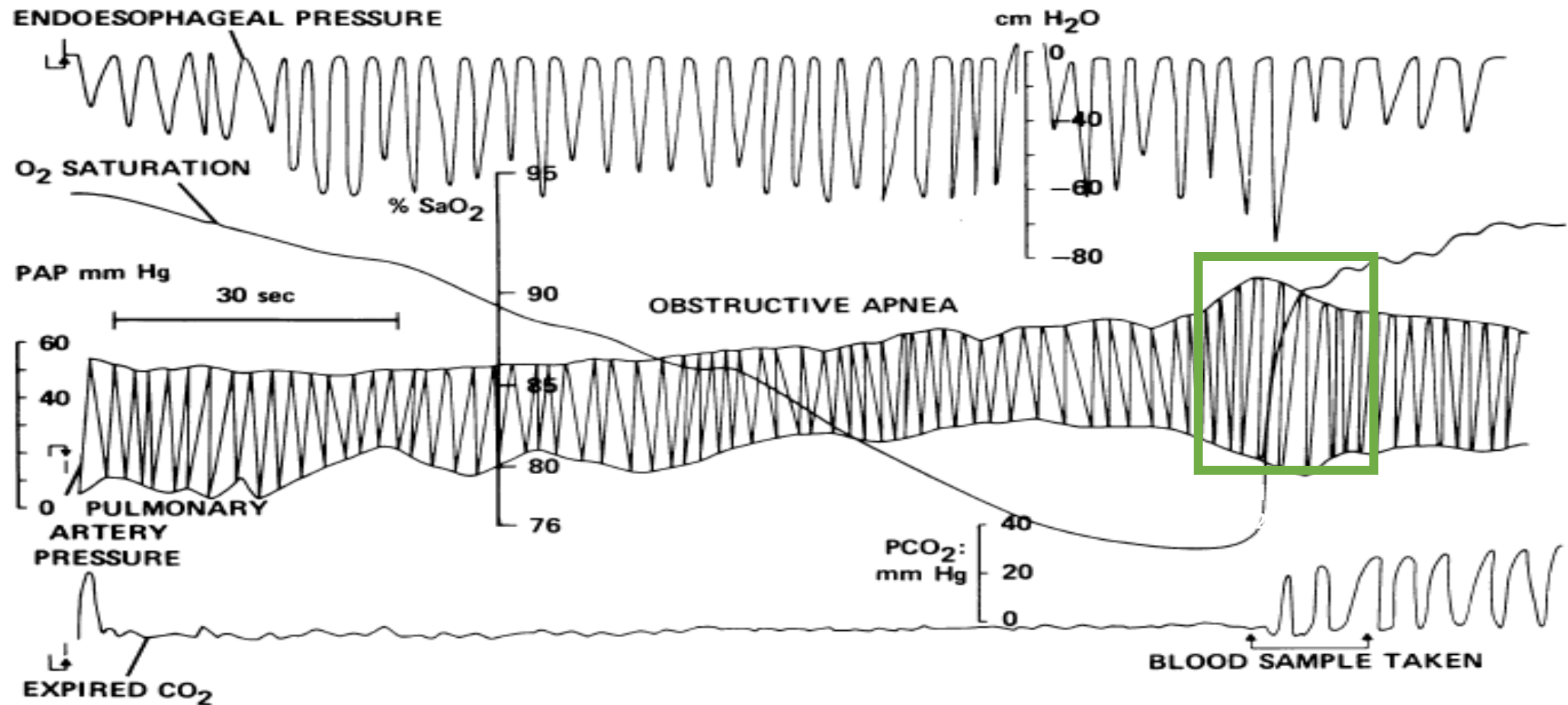


Hemodynamic changes in Obstructive Sleep Apnea

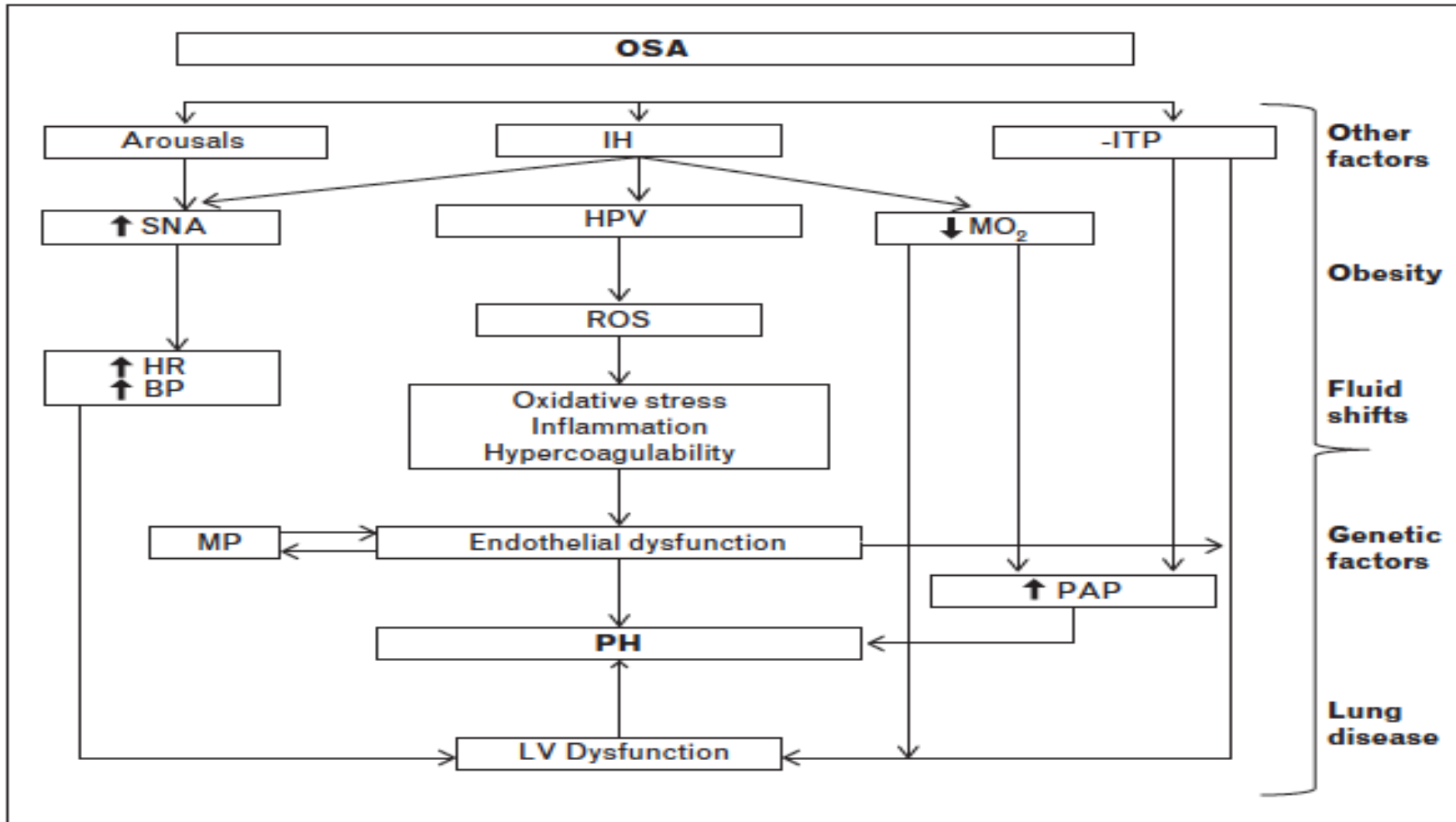


- Increases in systemic arterial blood pressure (SABP)
- Increases in PAP
- Increases in right atrial pressure (PRA)
- Further increase after arousal

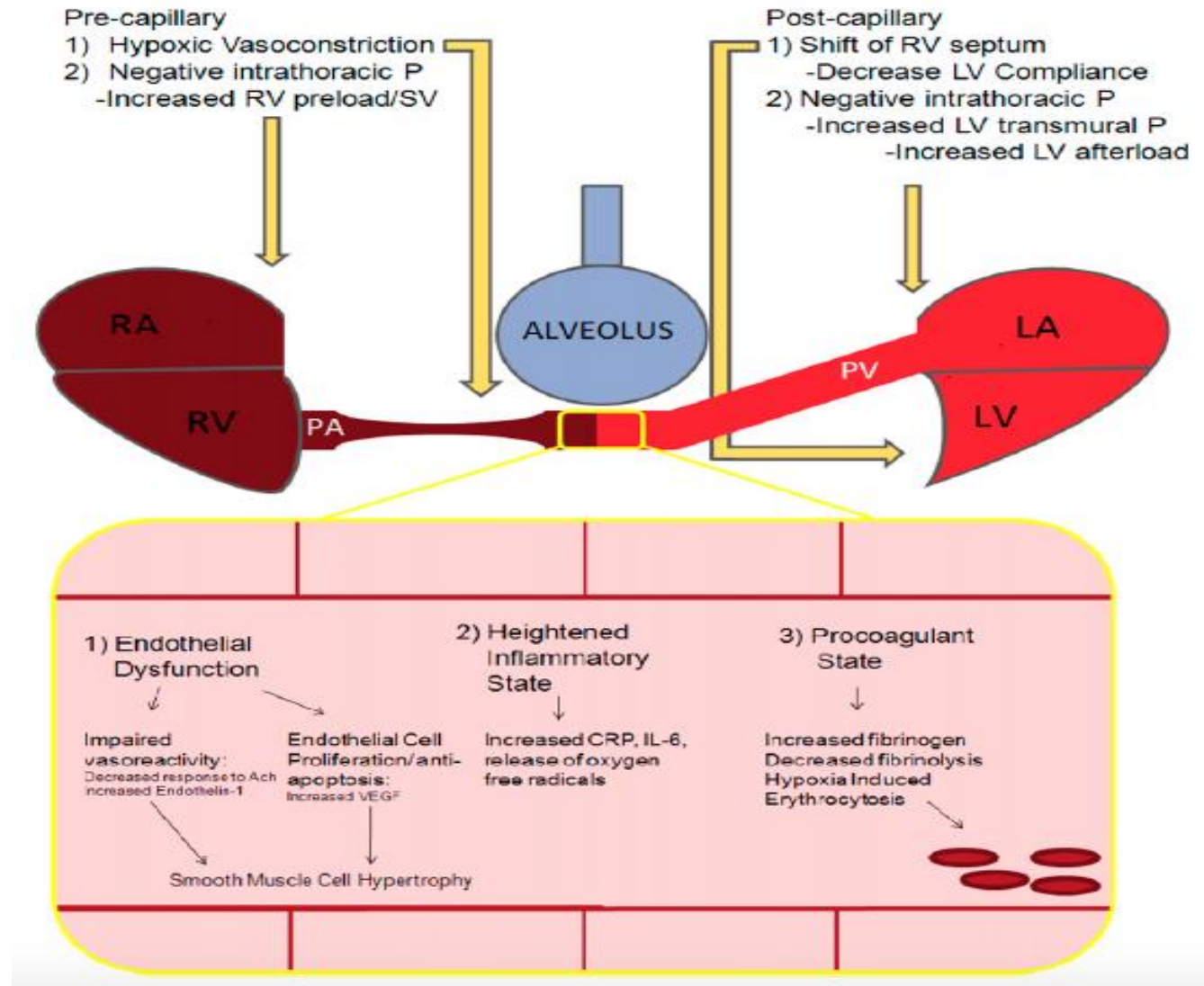
Hemodynamic changes in Obstructive Sleep Apnea



Pathophysiological Interactions of Obstructive Sleep Apnea and Pulmonary Hypertension

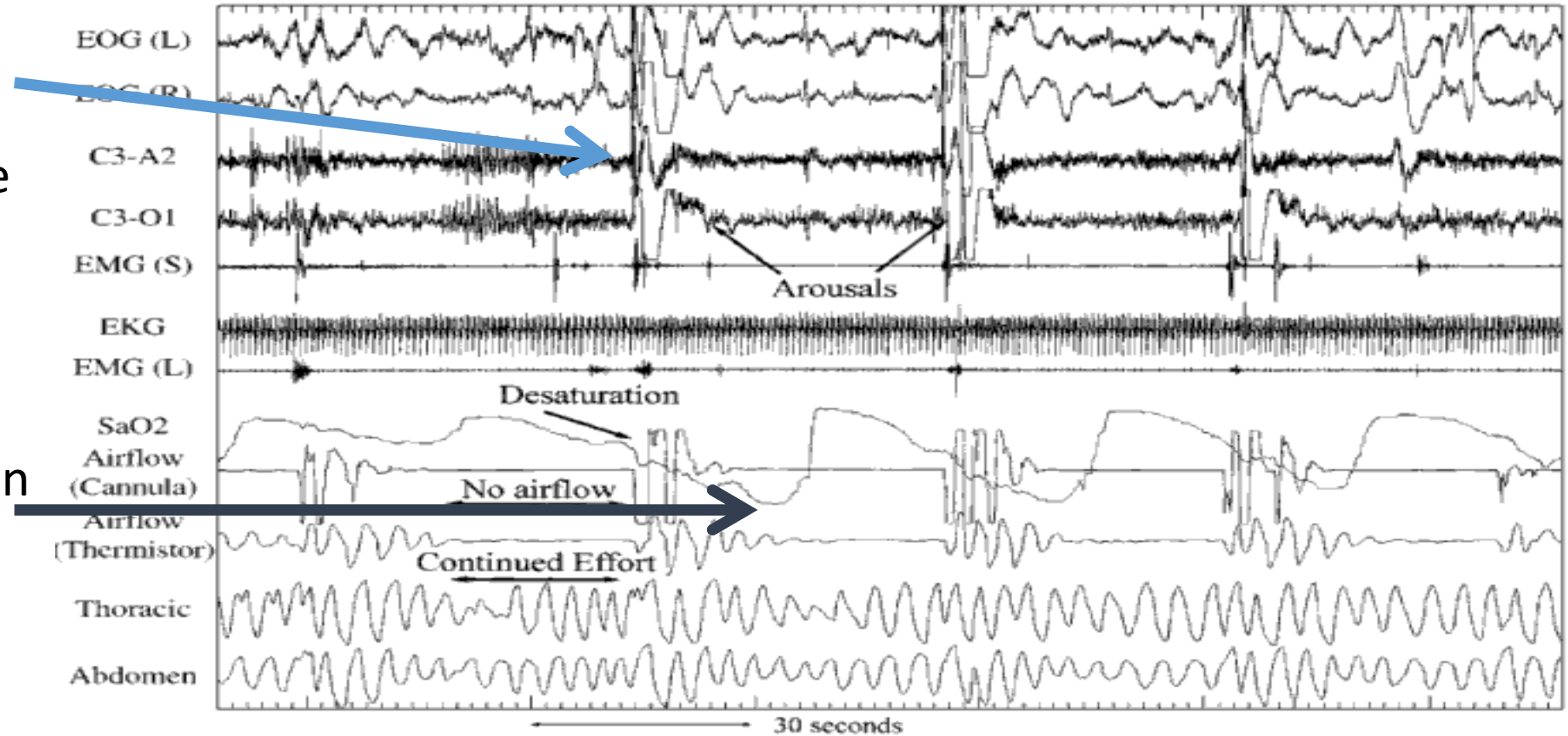


Pathophysiological Interactions of Obstructive Sleep Apnea and Pulmonary Hypertension

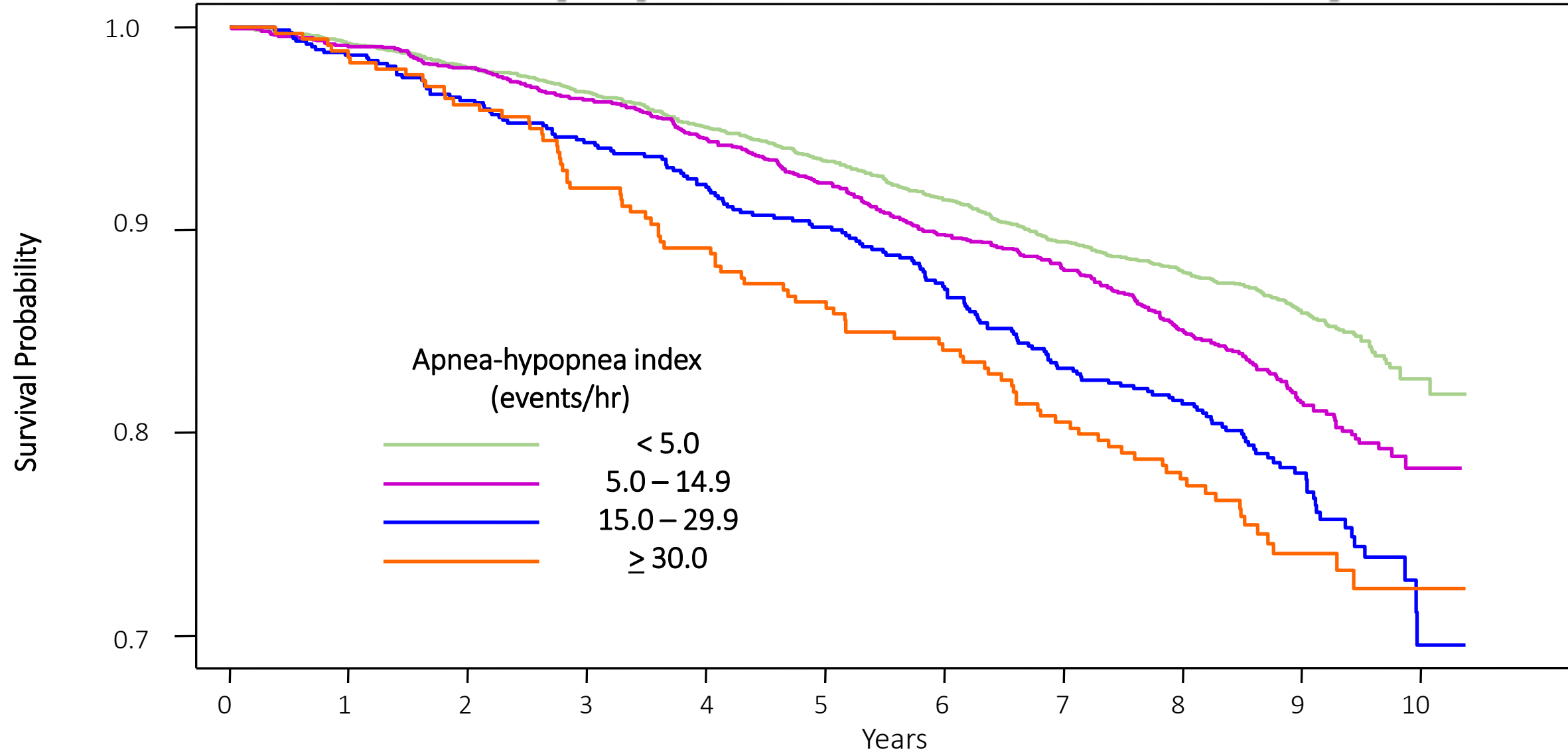


Consequences of Untreated Sleep Apnea

- Autonomic Nervous System Disturbances
- Intrathoracic Pressure Alterations
- Hypercapnia
- Intermittent Hypoxia
- Systemic Inflammation and Oxidative Stress



Obstructive Sleep Apnea and All-Cause Mortality



Numbers at risk:	6294	6205	6110	6001	5868	5732	5566	5411	4756	2357	300
Total Deaths:	0	59	143	241	359	478	616	757	875	989	1046

Prevalence of Sleep Apnea in patients with Pulmonary Hypertension: 11-89%

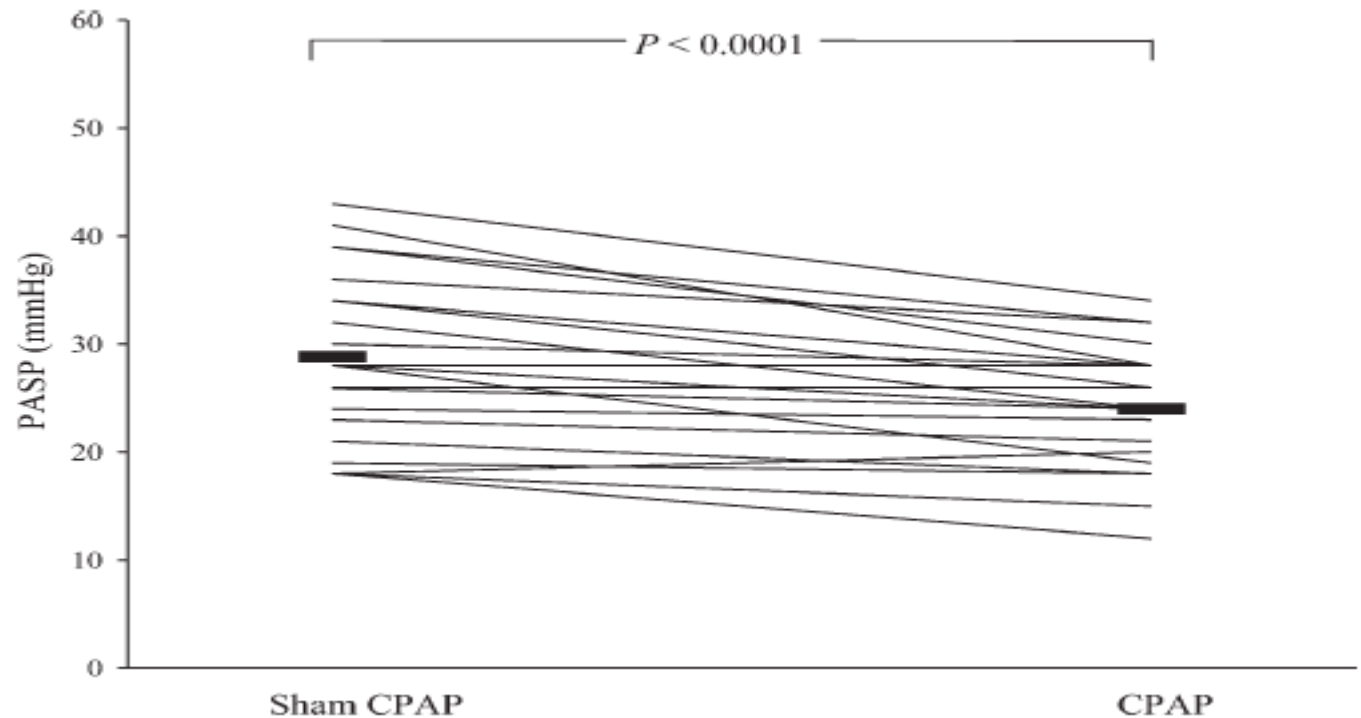
Study/year/type	N	Diagnosis of PH	Type of SDB	Prevalence of Sleep Apnea (%)	BMI, kg/m ²
Jilwan et al/2013 (prospective)	46	mPAP >25 mm Hg PCWP <15 mm Hg IPAH or CTEPH	AHI >5/h Nocturnal hypoxemia (time SaO ₂ <90%) >60 min	OSA: 41 (89) CSA: 4 (8) Nocturnal hypoxemia: 38 (82)	24.6±4.2
Prisco et al/2011 (prospective)	28	mPAP >25 mm Hg PCWP <18 mm Hg Groups I, IV, V	AHI >5/h Nocturnal hypoxemia (%TST SaO ₂ <90%)	OSA (AHI >5) 14 (50) CSA: 0 %TST <90%: SaO ₂ 30.6±36	31.3±9.3
Ulrich et al/2008 (prospective)	38	mPAP >25 mm Hg PCWP <15 mm Hg	AHI >10/h Nocturnal hypoxemia (>10% TST-SaO ₂ <90%)	CSR/CSA: 15 (39) OSA: 4 (11) Nocturnal hypoxemia (68)	25 (range, 22-29)
Schulz et al/2002	20	NR (mPAP 56±2.7 mm Hg)	CSR AHI >5/h	CSR 6 (30) OSA: 0	23.5±1.1
Rafanan et al/2001 (retrospective)	13	mPAP >25 mm Hg (rest) mPAP >30 mm Hg (exercise)	AI >5 Nocturnal Hypoxemia >10% TST-SpO ₂ <90%	0 with AI>5 10 (77) nocturnal hypoxemia	30.1±7.3

Limitations of Existing Data

- Different patient populations studied
- Small sample sizes
- Retrospective nature of the studies
- Outdated definition of pulmonary hypertension
- Lack of consideration of concurrent heart and lung disease
- Pulmonary hypertension is usually mild < 40 mm Hg

Effects of CPAP on Pulmonary Arterial Pressures

- Randomized, cross-over trial
- Individual values for the PASP after both sham and CPAP in patients with OSA
- Black bar represents mean PASP, changing from baseline 28.9 ± 8.6 mm Hg to 24.0 ± 5.8 mm Hg after 12 wk of CPAP ($P = .0001$)



Higher reduction in PASP after effective CPAP therapy was observed in OSA patients with either LV diastolic dysfunction (7.3 ± 3.3 vs. 1.6 ± 1.8 mmHg, $P = 0.001$) or PH at baseline (8.5 ± 2.8 vs. 2.6 ± 2.8 mmHg, $P = 0.001$)

Sleep Apnea Diagnostic Options

- Device Types
 - Type 1: classic in-lab, attended overnight multichannel device
 - Type 2: similar device as type1 but unattended at home
 - **Type 3: truncated home device providing 4-7 variables. No EEG so cannot detect arousals or quantify the denominator**
 - Type 4: 1-2 variables, typically oximetry and/or airflow

Home Sleep Apnea Testing (HSAT)

- Advantages

- Convenience
- Cost
- Comfort
- Availability
- Potential “representativeness” of testing in usual environment (little “first night” effect)

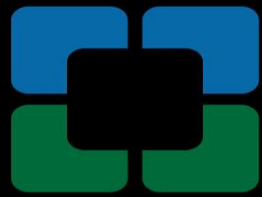
- Disadvantages

- Less data (particularly arousals with type 3)
- Inability to detect central events
- Limited access to raw data
- Failure rate (3-33%)
- **Under-estimate AHI by 12%**
- Use in heart failure and complex health conditions not proven
- May be more challenging in certain home environments
- Quality Control key!

Under-estimation of AHI by HSAT compared to PSG

Summary

- Prevalence of pulmonary hypertension with OSA is difficult to estimate (17-52%)
- High body mass index, higher levels of hypoxia/hypercarbia may be associated with higher prevalence of PH in the OSA population
- CPAP improves hemodynamics in patients with obstructive sleep apnea and concurrent pulmonary hypertension
- **PVDOMICS multicenter study poses a unique and unprecedented opportunity to examine the inter-relationships of sleep apnea and pulmonary hypertension subtypes as well as genomics and proteomics**



Cleveland Clinic

Every life deserves world class care.