

Obstructive Sleep Apnea Implications for Cardiac & Vascular Disease

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Sleep Apnea: Definitions

- Breathing cessation/reduction >10 s. in sleep
- Obstructive
- Central
- Apnea Hypopnea Index:
 - number of respiratory events per Hour
- AHI 5-15 Mild
- AHI 15-30 Moderate
- AHI >30 Severe

Sleep Apnea: Prevalence

- 15-20 % of adults have OSA (AHI >5 /Hr)
- 7% have at least a moderate OSA (AHI>15Hr)
- obesity
- over 40
- male gender

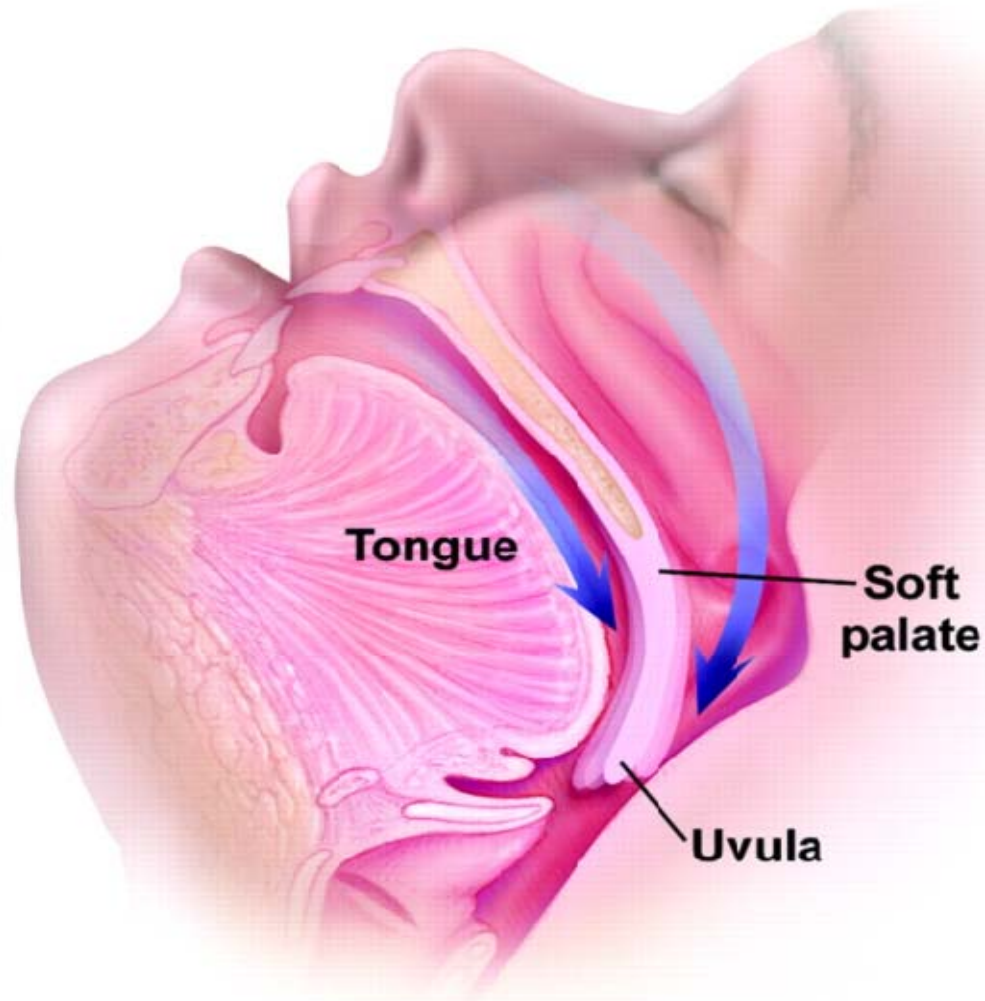
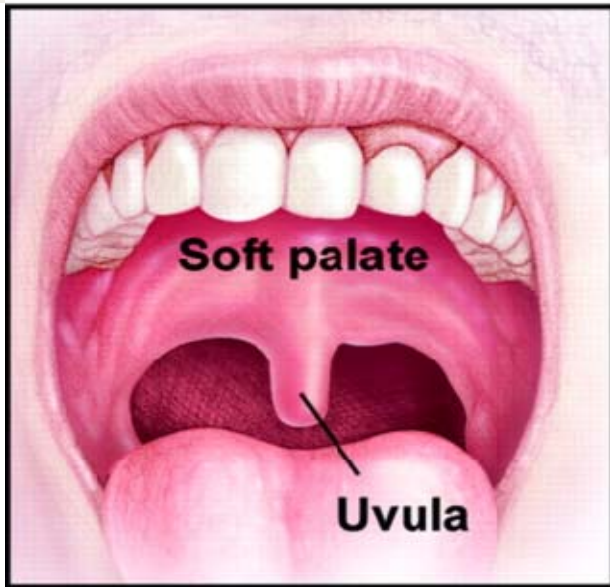


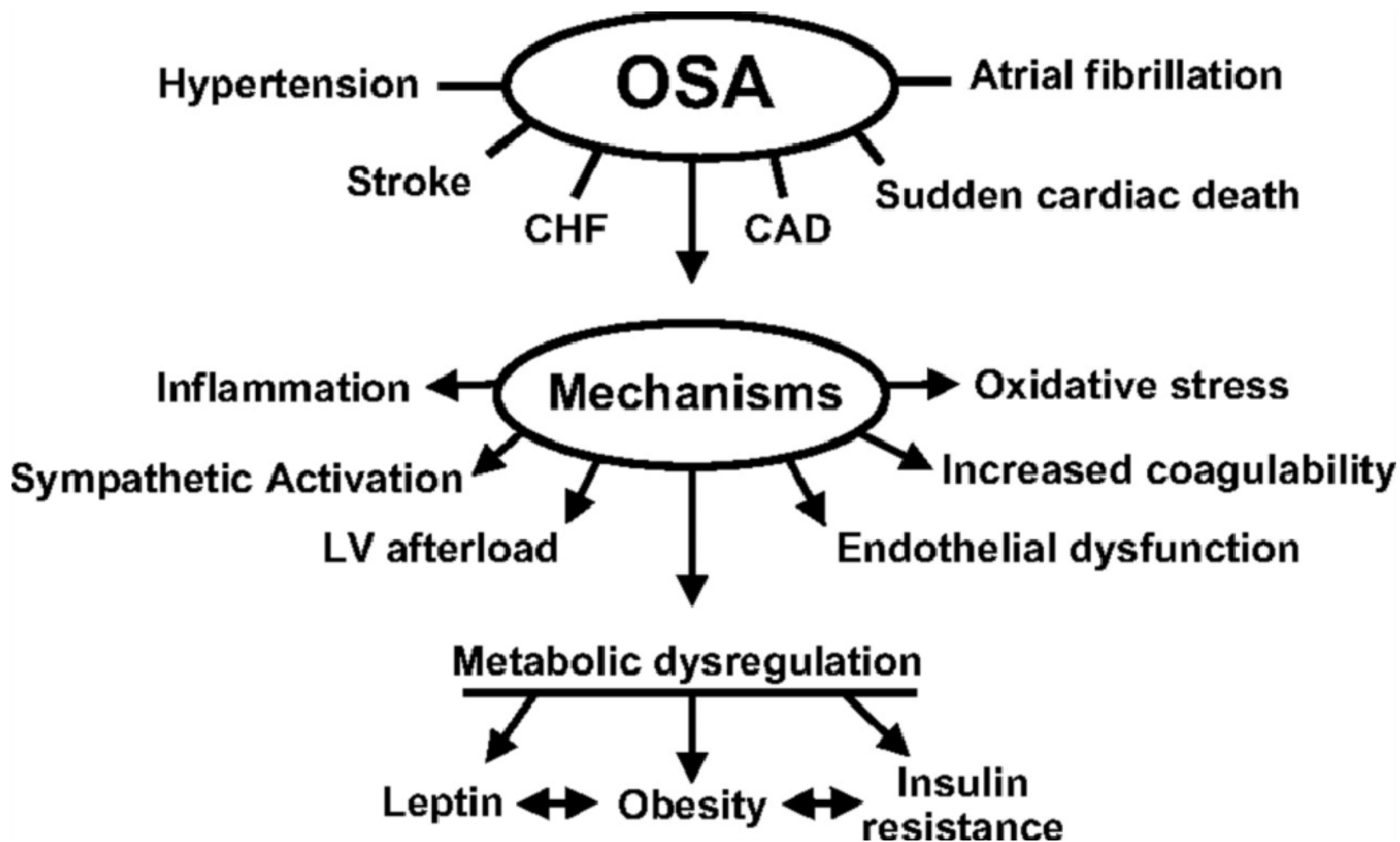
Illustration of the upper airway. During inspiration there is activation of pharyngeal dilator muscles that elicits the heightened muscular activity necessary to maintain airway patency. Reproduced with permission from Mayo Clinic Foundation.

Clinical Features of OSA

- Daytime sleepiness
- Non-restorative sleep
- Witnessed apneas
- Awakening with choking
- Nocturnal restlessness
- Insomnia/ freq. awakening
- Poor concentration
- Cognitive dysfunction
- Change in mood
- Morning headaches
- Nocturia
- Obesity
- Snoring
- Large neck circumference
- Narrow/crowded airway
- Polycythemia
- GERD
- Erectile dysfunction
- HTN
- CAD
- Cardiac arrhythmias
- Cor pulmonale
- Cerebrovascular disease

Clinical Cardiovascular Disease & OSA

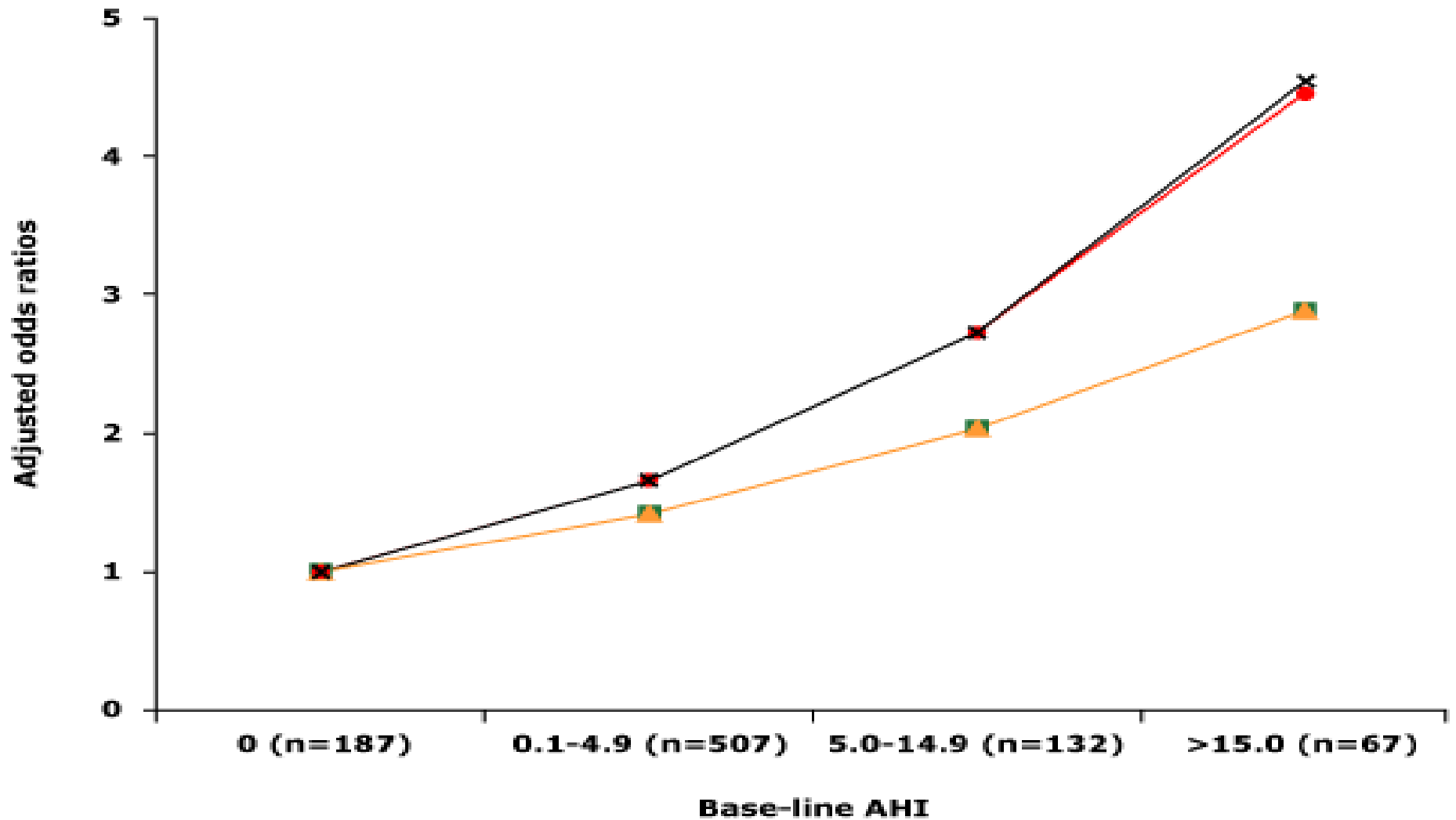
- HTN
- ARRHYTHMIA
- CARDIAC ISCHEMIA
- HEART FAILURE
- SUDDEN DEATH
- PULMONARY HTN
- STROKE



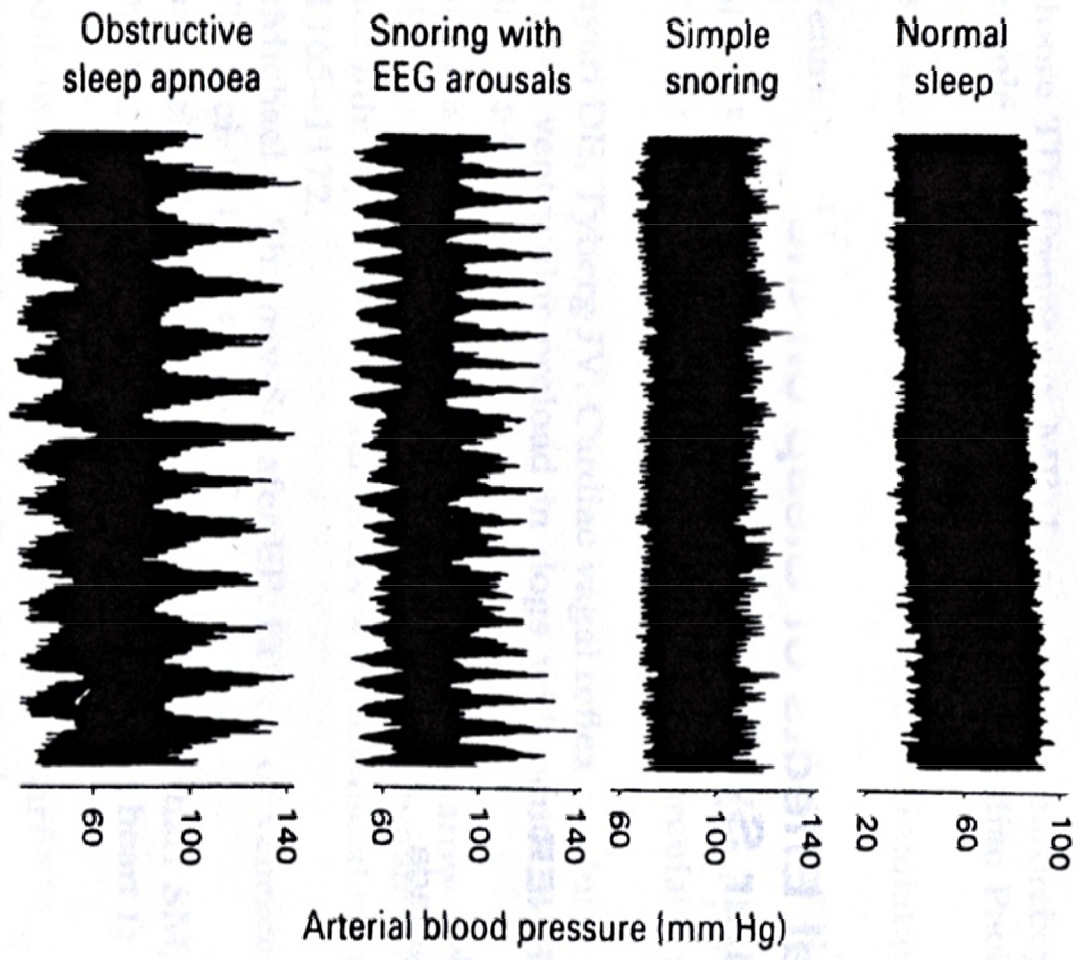
Clinical Cardiovascular Disease & OSA

■ HYPERTENSION

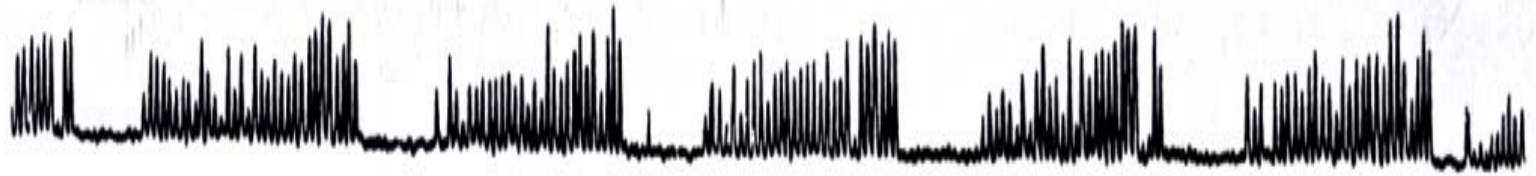
- Association HTN & OSA well established
- High incidence of OSA in refractory HTN
- Risk in a dose-response manner
- Nighttime BP “Dipping” is lost in OSA
- CPAP ↓ BP in OSA pt. & refractory HTN



- ✱ Adjusted OR for base-line HT status
- Adjusted OR for base-line HT status and nonmodifiable risk factors (age and sex)
- ▲ Adjusted OR for base-line HT status, nonmodifiable risk factors, and habitus (BMI and waist and neck circumference)
- Adjusted OR for base-line HT status, nonmodifiable risk factors, habitus, and weekly alcohol and cigarette use



SNA



RESP



BP



Control Subject

Severe OSA Patient

ECG



HR

64 beats/min

82 beats/min

BP, mm Hg

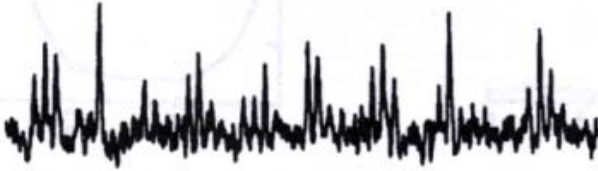
140
120
100
80
60



140
120
100
80
60



Neurogram



Respiration



10 sec.

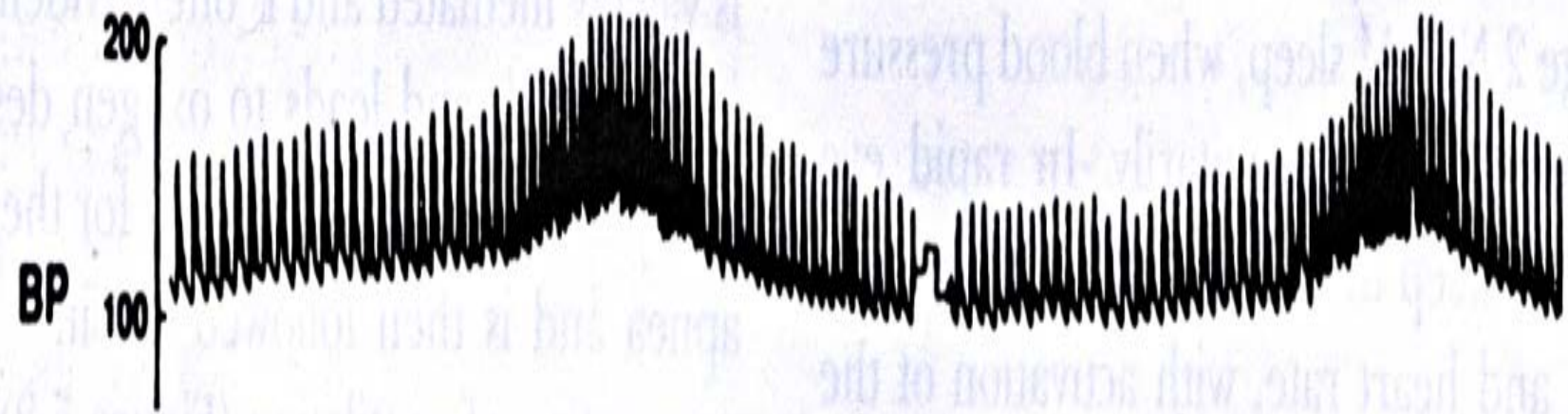
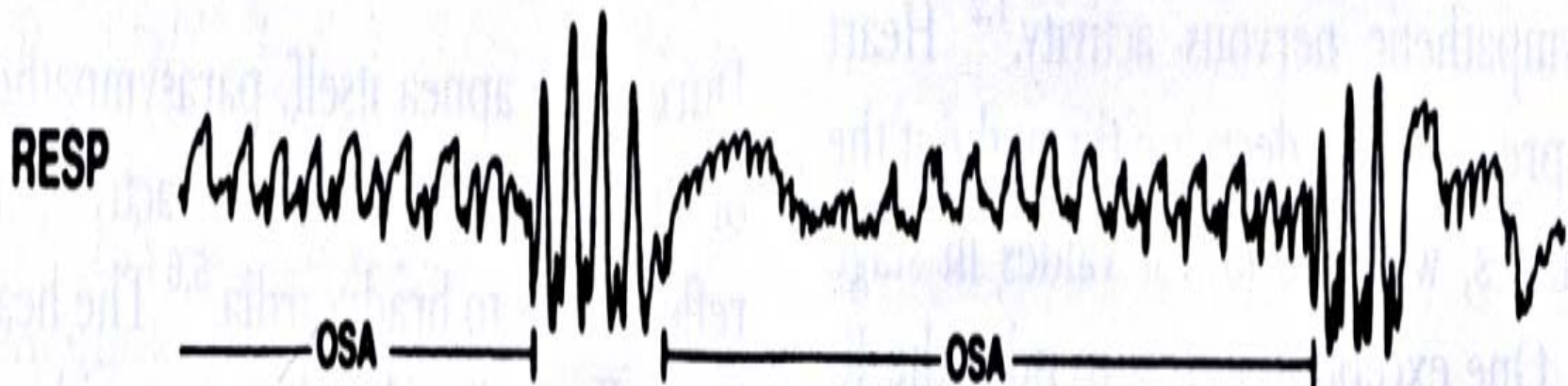
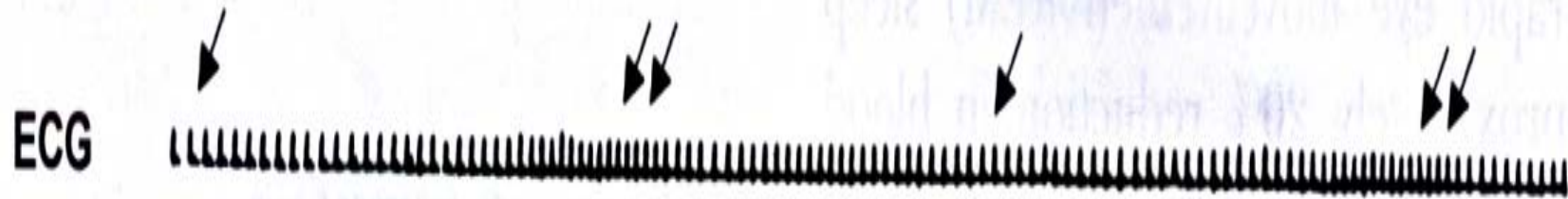
Cardiovascular effects of OSA

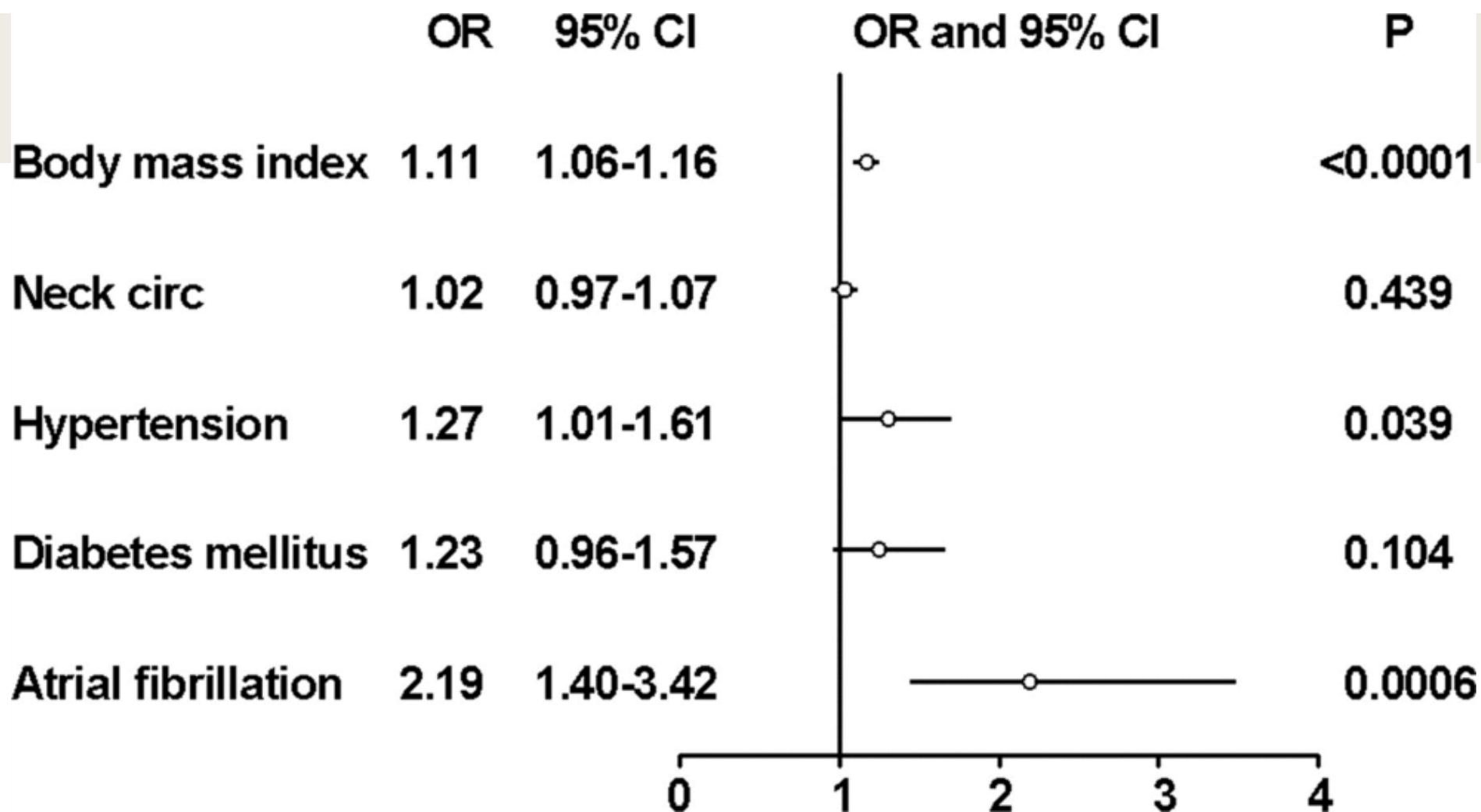
- **BP changes**
 - Cardiac preload reduced (impaired venous return)
 - “ ” afterload increase (vasoconstr. hypoxemia)
- **HR Brady-Tachy: “diving reflex”**
- **Arousals (<15 sec.):**
 - Rise in Systolic ~ 20 mm Hg
 - “ in Diastolic ~ 15 mm Hg
 - “ in HR ~ 10 b/min

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■ **ARRHYTHMIAS**

- **Cyclic Heart Rate Variation during OSA**
- **Brady-Tachyarrhythmia**
- **Atrial Fibrillation**
 - 50% of A.Fib pt. are at risk for severe OSA
 - High Recurrence of A.Fib after cardioversion in OSA
- **PVCs (very common)**
- **Ventricular Tachycardia (very rare)**





Association between AF and OSA, with adjusted odds ratio (OR) and 95% CI for the association between AF and OSA. After adjustment for BMI, neck circumference (neck circ), hypertension, and diabetes mellitus, AF is significantly associated with OSA (odds ratio, 2.19; $p = 0.0006$). Reprinted from Gami et al. *Circulation* 2004; 110:364, with permission of Lippincott, Williams & Wilkins.

Obstructive Sleep Apnea[†]: Implications for Cardiac and Vascular Disease

Chest. 2008;133(3):793-804. doi:10.1378/chest.07-0800

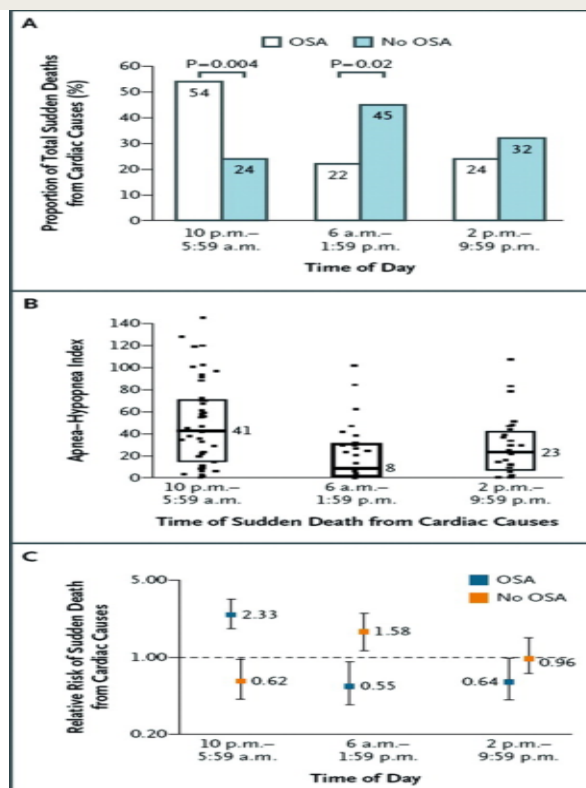
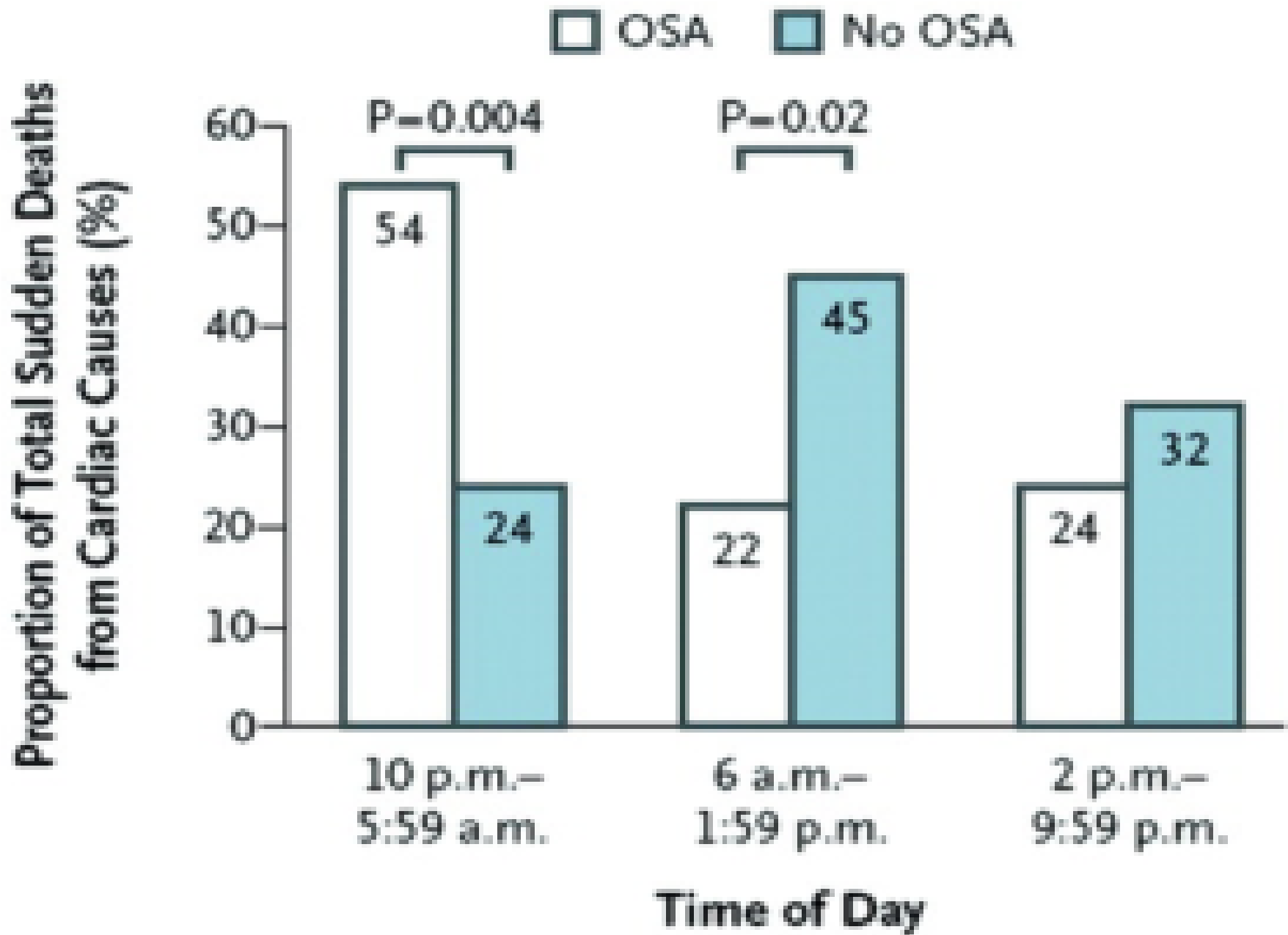
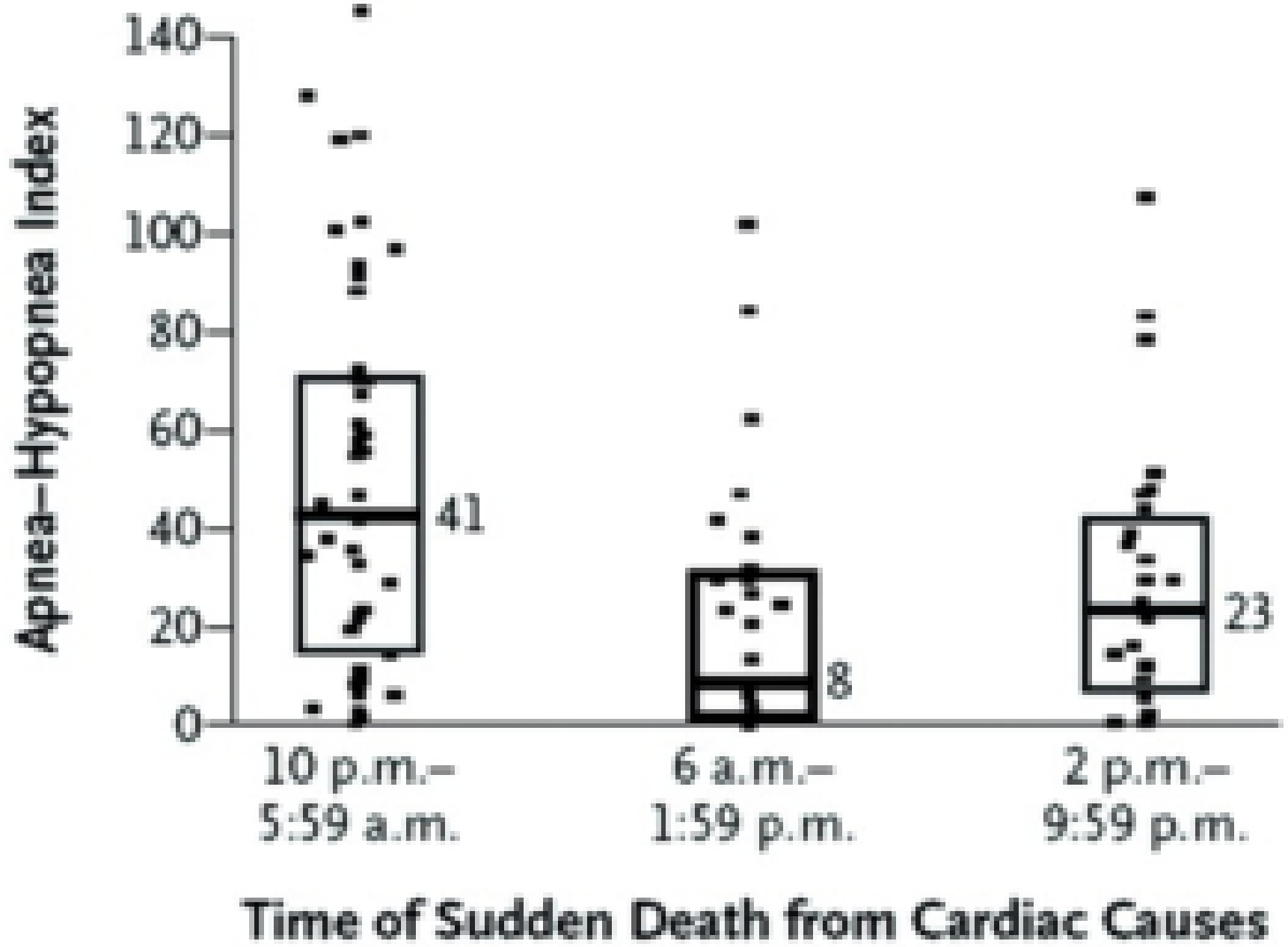


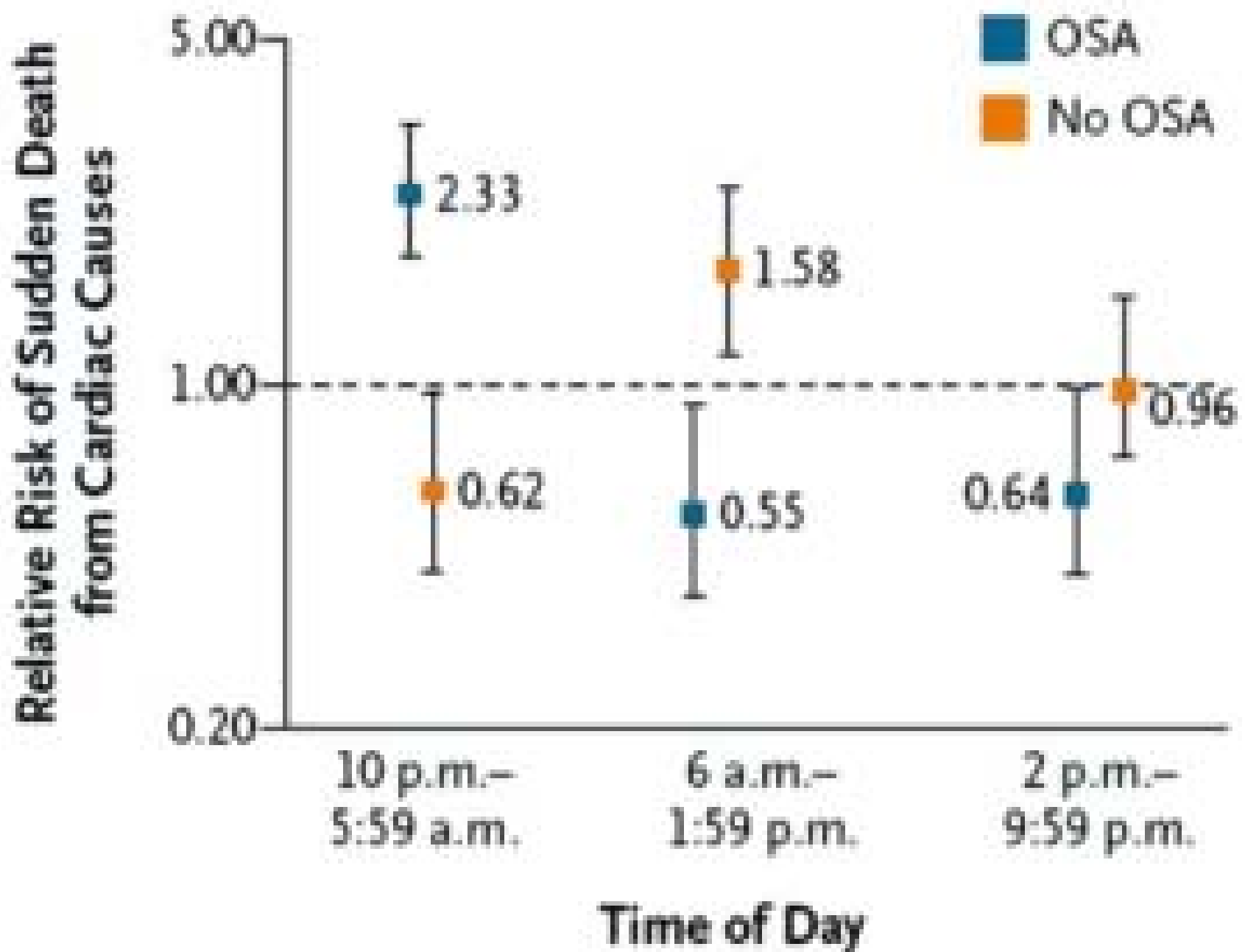
Figure Legend:

Sudden death from cardiac causes according to usual sleep-wake cycles. Top, A: Day-night patterns of sudden death from cardiac causes on the basis of 8-h time intervals for 78 persons with OSA and 34 persons without OSA. Center, B: AHI for persons with sudden death from cardiac causes during 8-h intervals. The line within each box represents the median AHI, and the box represents the interquartile range (25 to 75th percentiles). The figure includes data from persons with OSA and persons without OSA ($p = 0.001$) for the comparison of the AHI according to the time of sudden death. Bottom, C: Relative risk of sudden death from cardiac causes during 8-h intervals, as compared with the remaining 16 h of the day, for 78 persons with OSA and 34 persons without obstructive sleep apnea. The squares represent the relative risk point estimates, and the I bars indicate 95% CIs. Reprinted from Gami et al. *N Engl J Med* 2005; 352:1206–1214, with permission of the Massachusetts Medical Society.

A

B

C



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■ HEART FAILURE

- CSA in 40% of Systolic Heart Failure pt.
- OSA in 10% “ “ “
- CSA indicates poor prognosis
- CPAP in OSA: reduces BP & improves EF
- CHF worsen OSA thru airway soft tissue edema
- CPAP in CSA: no effect on mortality (CANPAP)

Clinical Cardiovascular Disease & OSA

- **HEART FAILURE & CSA**
 - **CANPAP study**
 - CPAP in CSA no effect on mortality
 - **Add hoc analysis identified subgroup of patients who may benefit**
 - **Recommendations: arbitrary use CPAP at 10 cm H₂O and determine response**

Clinical Cardiovascular Disease & OSA

- **CARDIAC ISCHEMIA**
 - OSA predictor for CAD & poor prognosis
 - OSA Treatment reduces risks for cardiac events
 - Etiological relationships needs confirmation
 - OSA cause nocturnal angina & ST depression
 - CPAP can successfully treat nocturnal angina
 - OSA pt. risk “nighttime Sudden death”

Clinical Cardiovascular Disease & OSA

- **PULMONARY HYPERTENSION**
 - Acute Hypoxemia induces Pulm. Vasoconstriction
 - Not known if OSA leads to Pulmonary HTN
 - CPAP has a modest benefit on Pulmonary HTN
 - Treatment is indicated if OSA is present

Clinical Cardiovascular Disease & OSA

■ STROKE

- High prevalence in OSA
- Relationship: not proven causal yet
- Snoring: independent predictor for stroke
- Brain MRI changes associated with OSA
- Stroke worsens preexisting OSA
- Severe OSA after stroke predicts early mortality
- Central apnea is usually a result of a stroke

Early diagnosis and treatment of obstructive sleep apnea after stroke

by Arielle P. Davis, Martha E. Billings, W.T. Longstreth, and Sandeep P. Khot

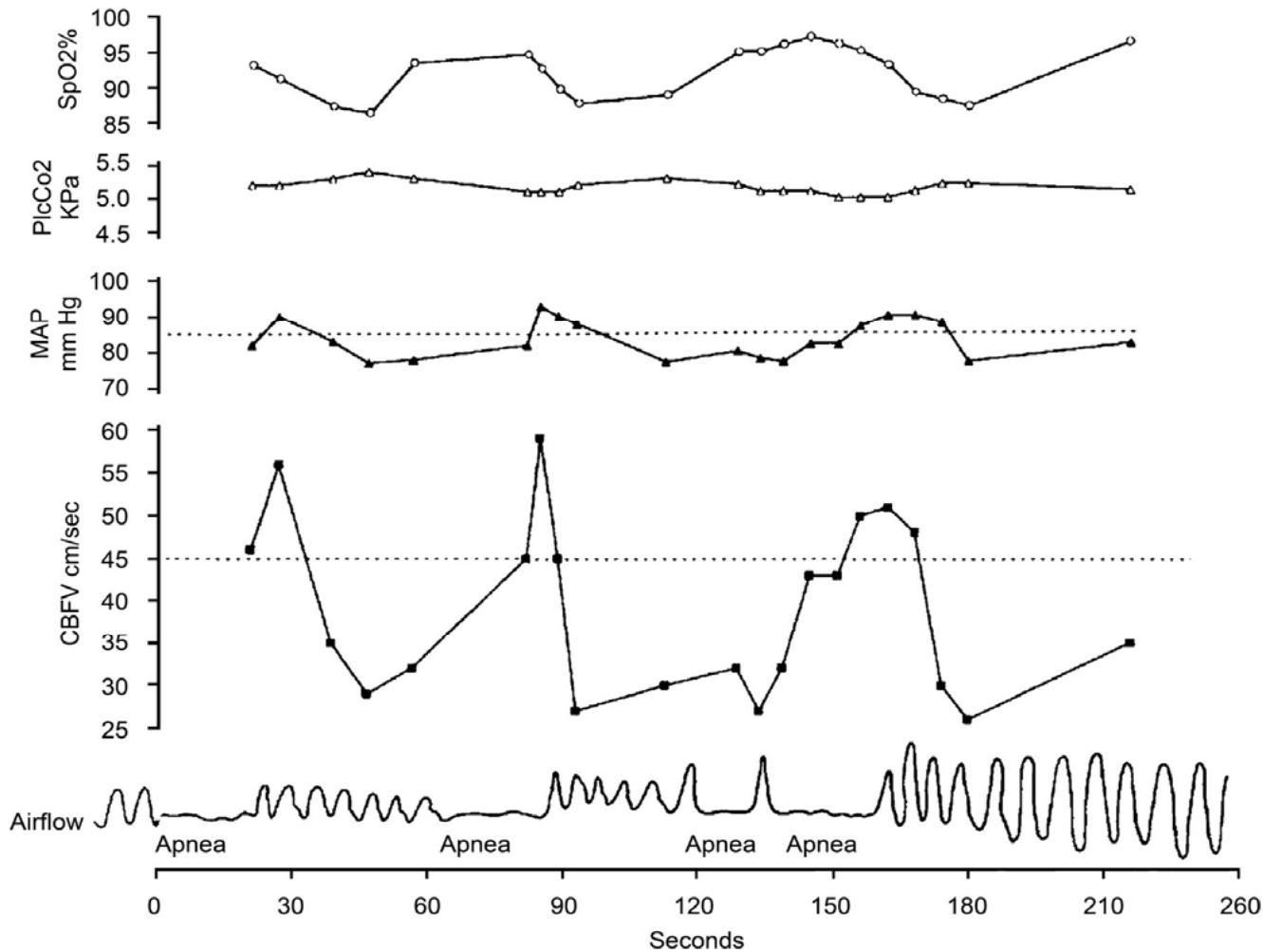
Neurol Clin Pract
Volume 3(3):192-201
June 10, 2013



OSA & Stroke

- Prevalence of OSA in stroke 50-70%
- OSA may predate, worsen & persist after stroke
- Predictor of poor outcome & mortality
- Mechanisms:
 - Reduced CBF
 - BP fluctuations
 - Hypoxemia
 - Impaired cerebral autoregulation
 - Sleepiness, cognitive dysfunction, increased length of stay and rehab.

Figure 2 Physiologic recordings in a patient with obstructive sleep apnea Simultaneous recordings of arterial oxygen saturation (SaO₂), transcutaneous arterial PCO₂ (PtcCO₂), mean arterial blood pressure (MAP), cerebral blood flow velocity (CBFV), and airfl...



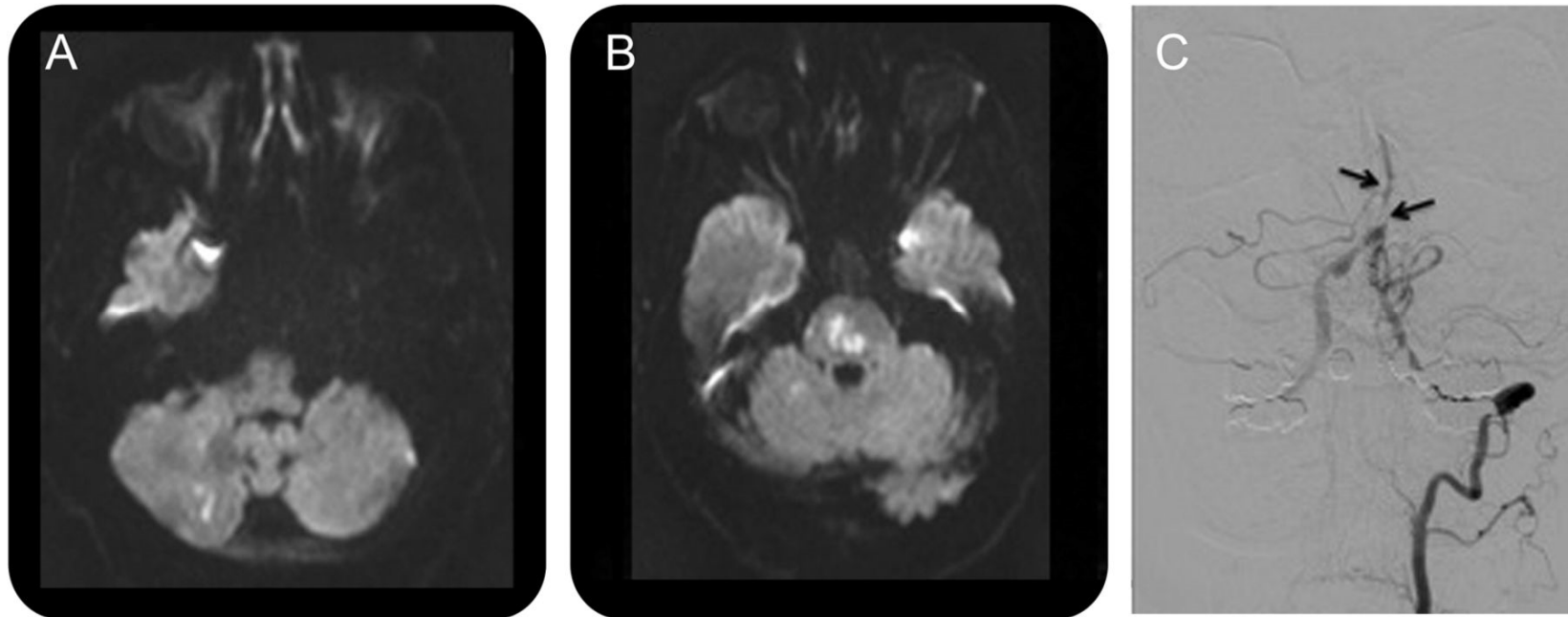
Davis A et al. *Neurol Clin Pract* 2013;3:192-201



Case Report

- 74 male presents with vertigo, nausea, ataxia.
- Hx of Stroke, DM, A.Fib, HTN, Hypercholest.
- Well controlled
- On ASA, Coumadin
- MRI: pons & cerebellar acute infarcts
- Angio: cerebral atherosclerosis.

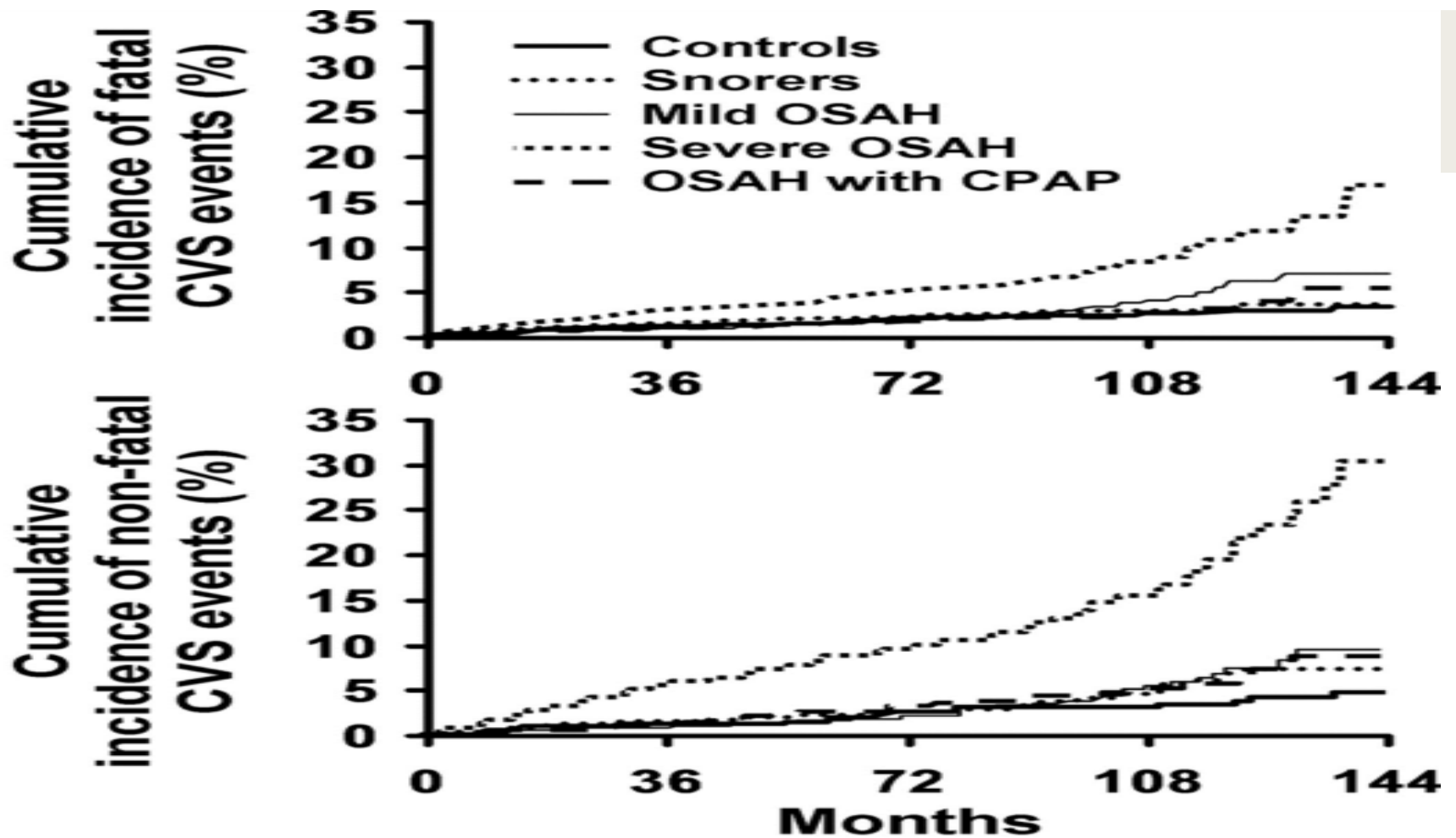
Figure 1 Imaging in case 1(A) Diffusion-weighted MRI demonstrates a right cerebellar infarct and (B) pontine infarcts.



Davis A et al. *Neurol Clin Pract* 2013;3:192-201

Case Report

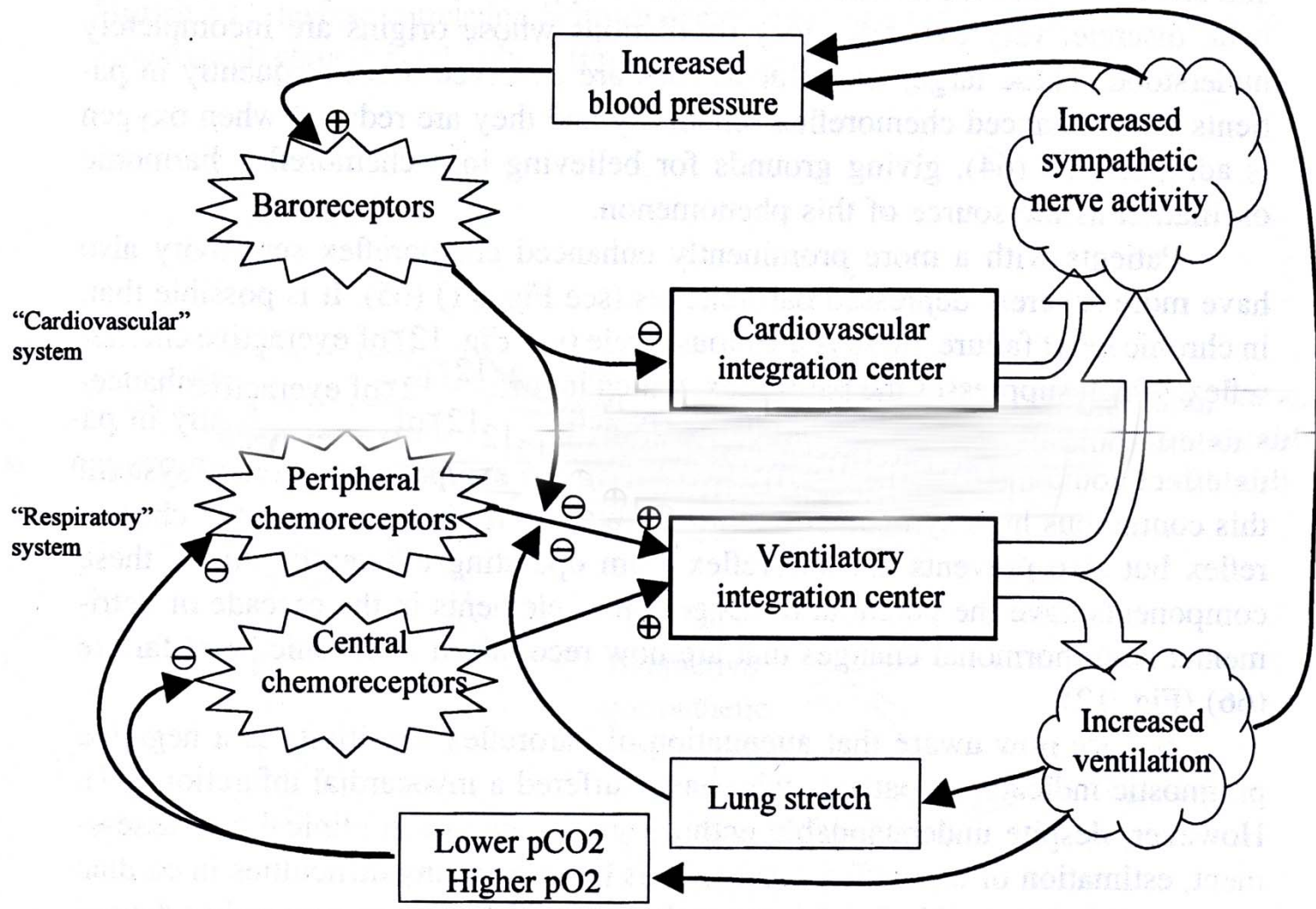
- 6 mos. recovered
- C/O of Sleepiness, poor concentration
- PSG: severe OSA (AHI=56)
- Symptoms improved on CPAP.
- No strokes after 2 years follow up.



Controls	264	262	259	258
Snorers	377	372	361	232
Mild OSAH	403	401	392	264
Severe OSAH	235	229	221	167
OSAHS with CPAP	372	364	361	229


MECHANISMS LEADING TO CARDIOVASCULAR PATHOLOGY IN OSA

- **Sympathetic Activation**
- **Vascular Endothelial Dysfunction**
- **Oxydative Stress & Inflammation**
- **Metabolic Factors**




Normal Autonomic cardiovascular responses to sleep

■ NREM Sleep

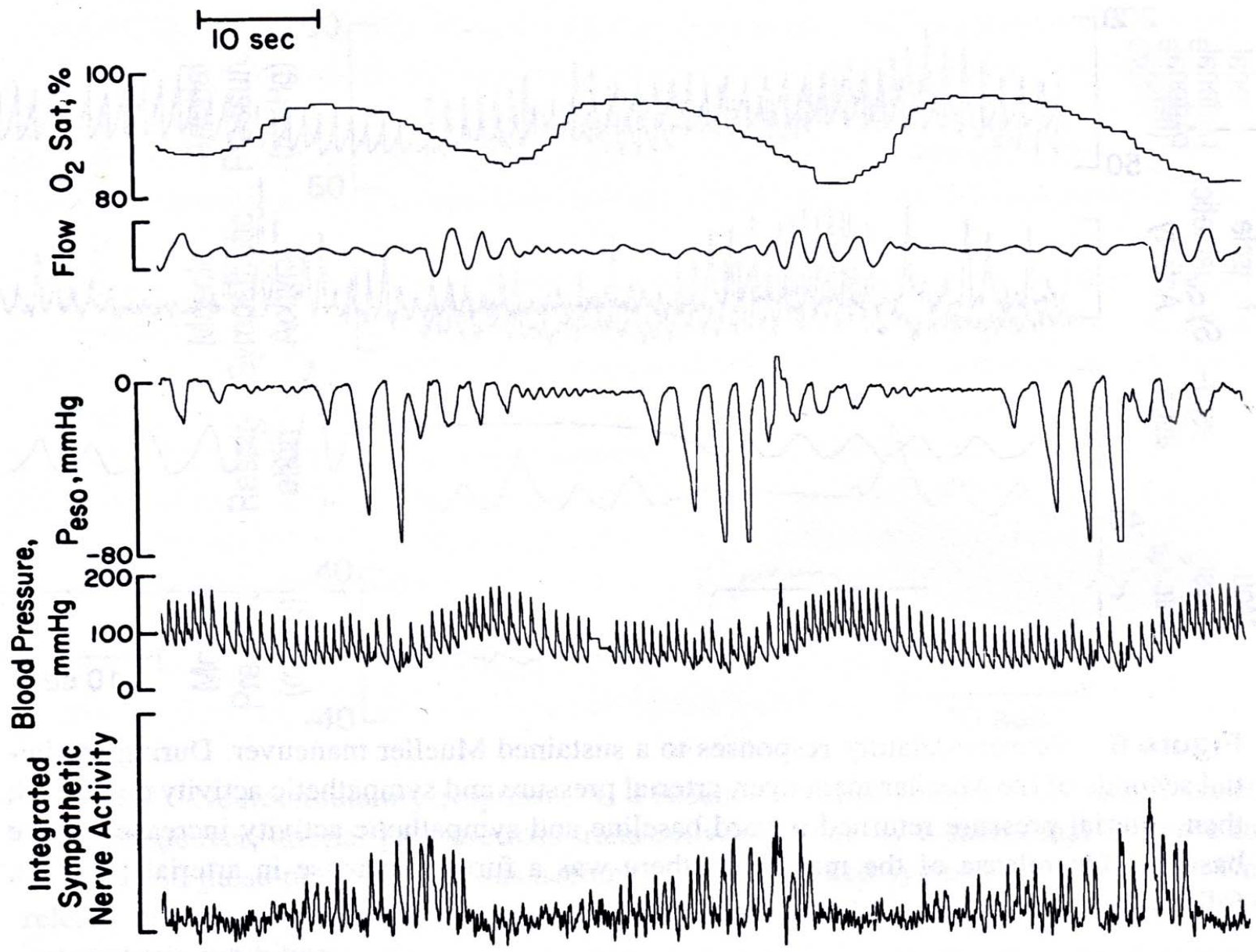
-  Sympathetic Activity
- 20% Drop in BP/HR (lowest in Delta)
- Exception “K complexes” of stage II

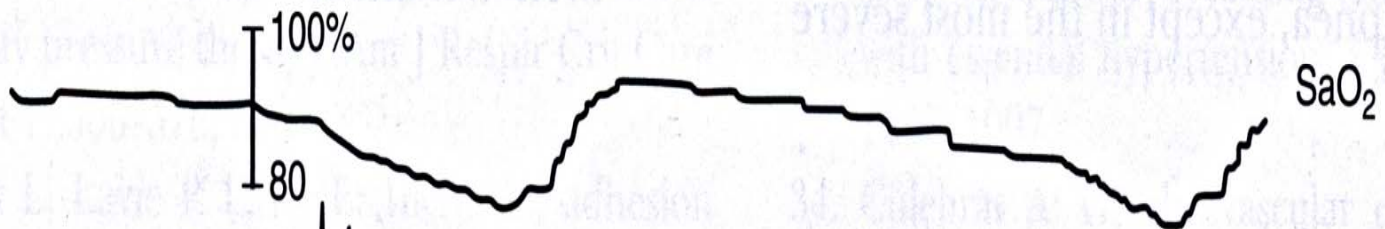
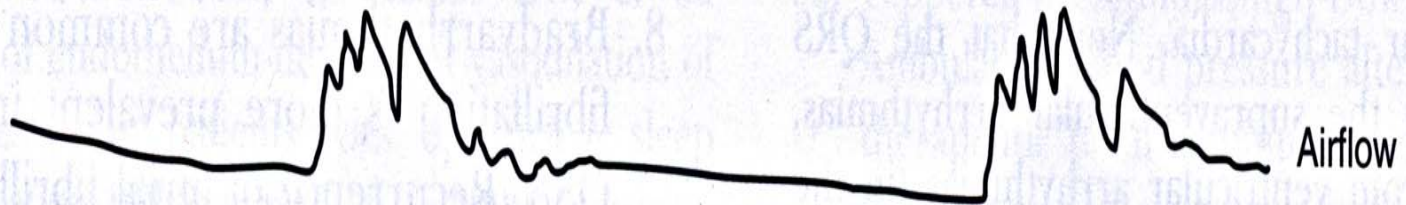
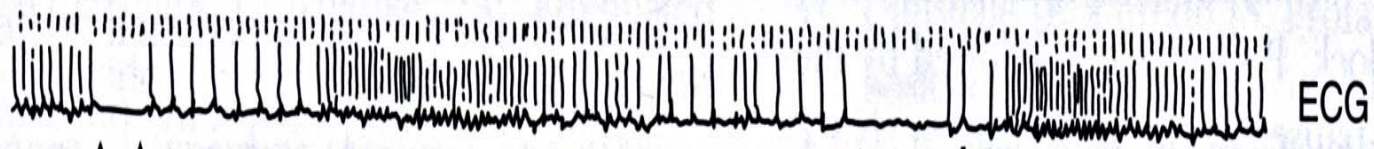
■ REM Sleep

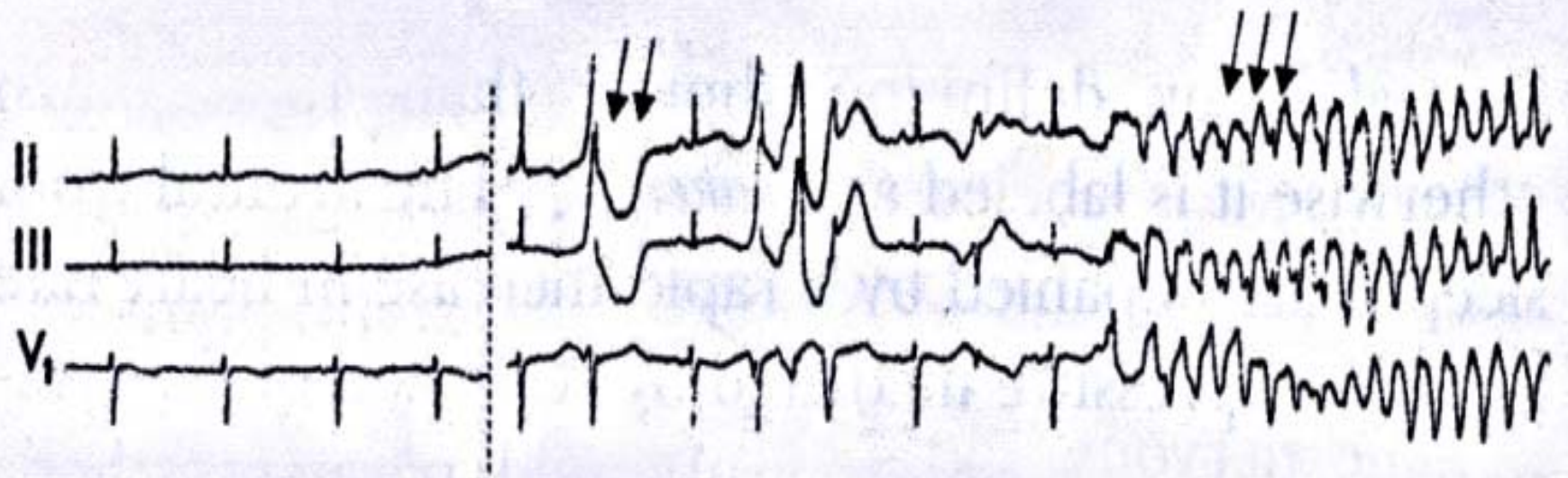
-  Sympathetic Activity (to near wakefulness)
- Increase in BP/HR
- Burst of Sympathetic Activity during phasic REM

MECHANISMS LEADING TO CARDIOVASCULAR PATHOLOGY IN OSA

- **Sympathetic Activation:**
 - O₂ desat. \Rightarrow Chemoreceptor \Rightarrow Sympathetic Act.
(Higher daytime BP and Heart Rate)
 - Heart Rate variability decreased (marker for HTN)
 - CPAP \Downarrow night & daytime Sympath. Act. in HTN







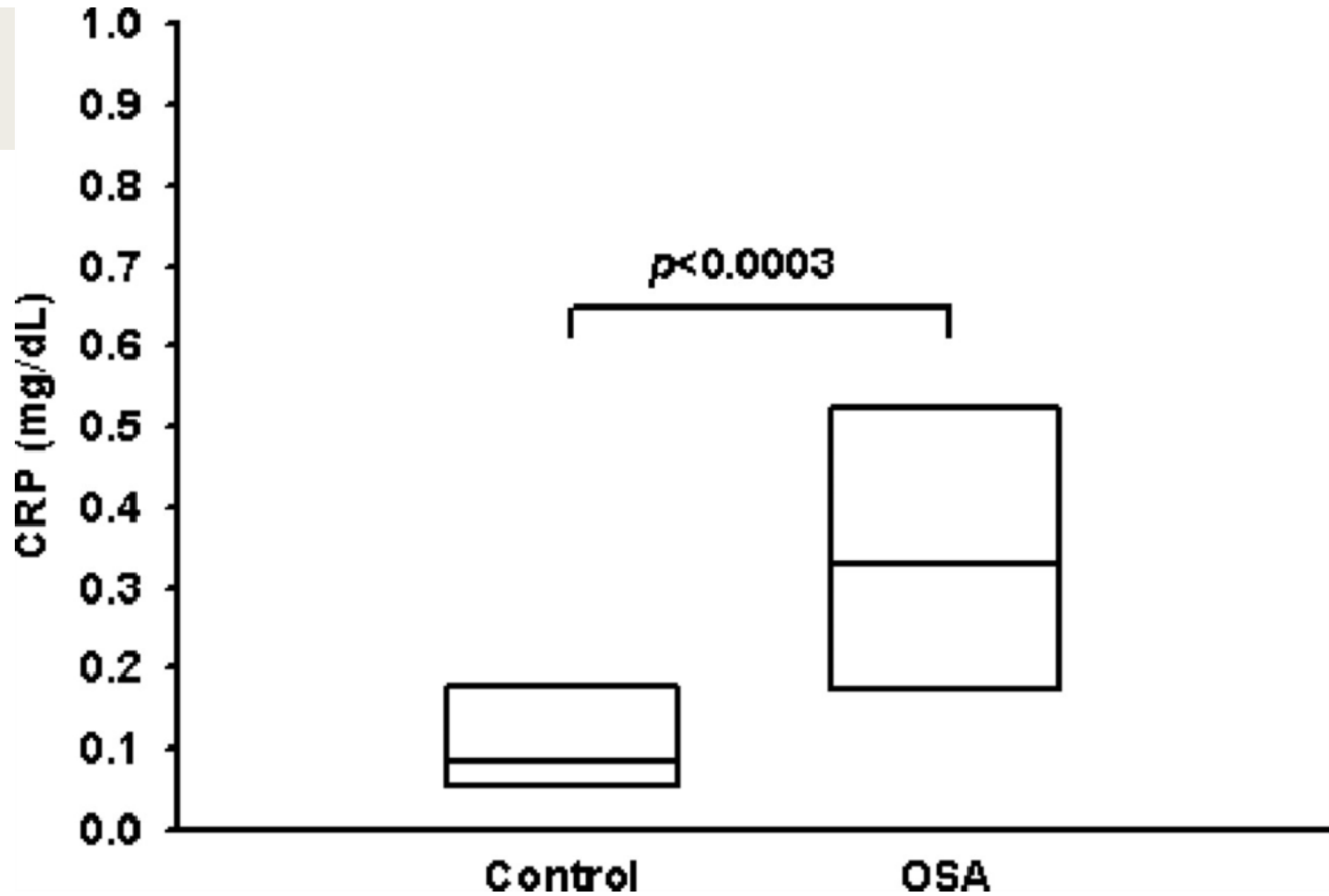
400 msec



MECHANISMS LEADING TO CARDIOVASCULAR PATHOLOGY IN OSA

■ OXIDATIVE STRESS & INFLAMMATION

- Repetitive apnea ⇒ Oxidative stress
- Oxygen radicals ⇒ Inflammation & tissue damage
- Chronic sleep deprivation ⇒ inflammatory cytokines
- CRP, TNF and inflammatory mediators are ↑ in OSA.
Levels correlate with the severity and ↓ by CPAP



MECHANISMS LEADING TO CARDIOVASCULAR PATHOLOGY IN OSA

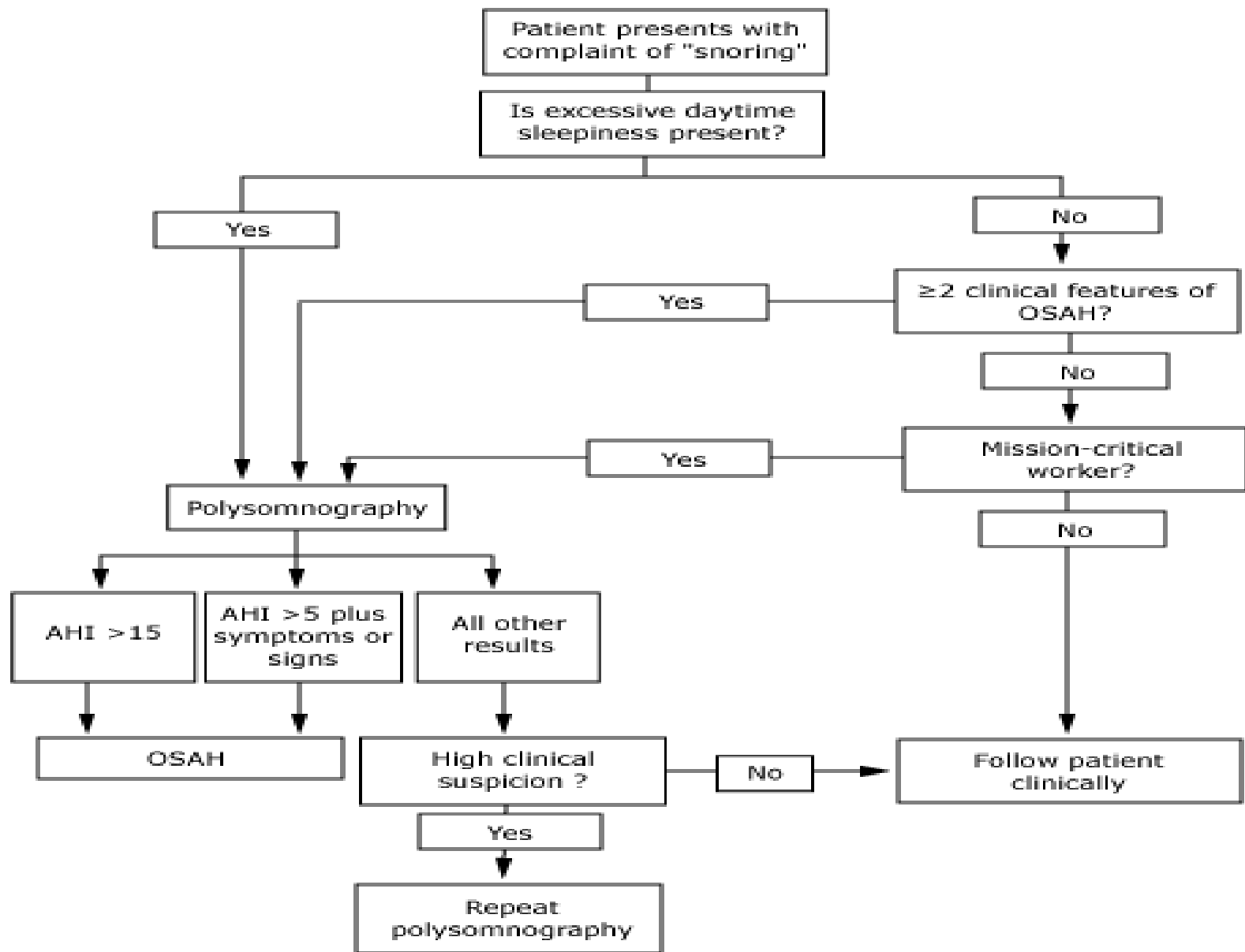
- **VASCULAR ENDOTHELIAL DYSFUNCTION**
 - In OSA impaired response to vasodilators
 - As seen in HTN, DM, Hyperlipidemia, Smokers
 - Suggestive of vessel resistance and possible indicator for future vascular disease

MECHANISMS LEADING TO CARDIOVASCULAR PATHOLOGY IN OSA

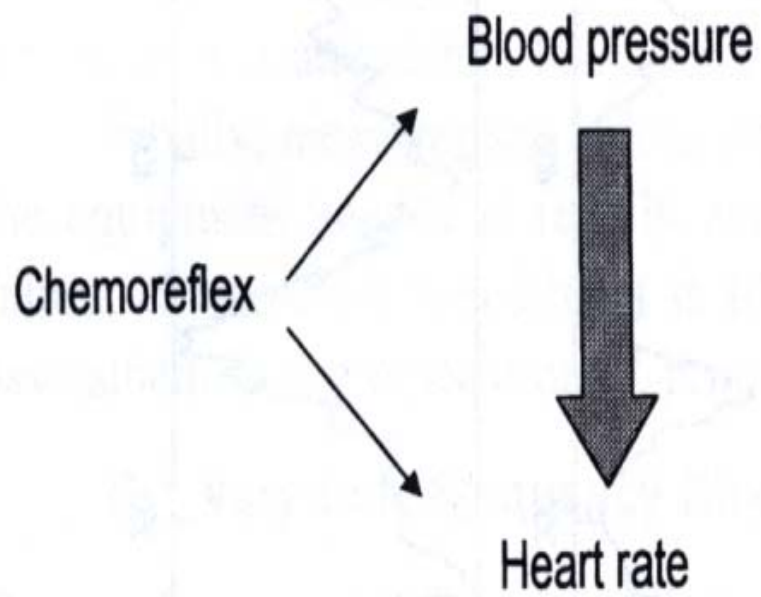
- **METABOLIC EFFECTS**
 - Glucose intolerance
 - Leptin resistance (i.e. increased level)
(appetite suppressant adipokine)
- **CPAP treatment**
 - Reduces Leptin level
 - Decreases Abdominal fat accumulation
 - Improves Glucose intolerance

SUMMARY

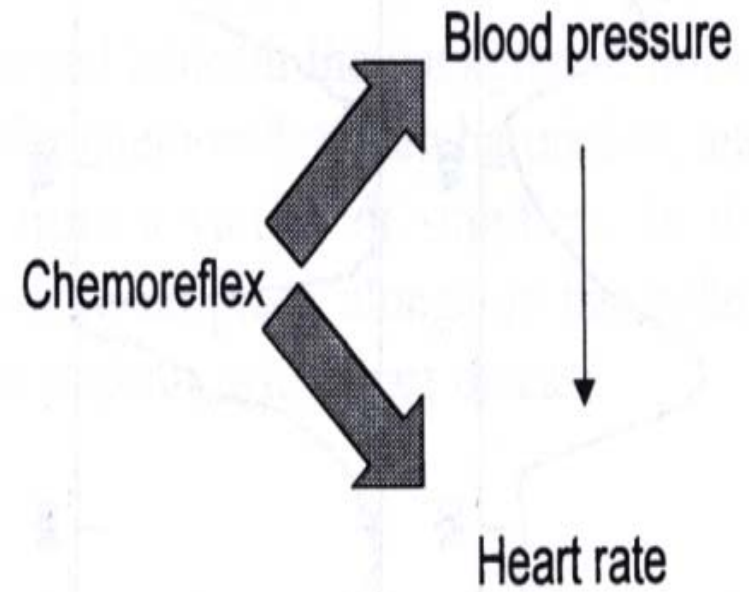
- **OSA associated with**
 - Systemic HTN
 - Mild pulmonary HTN (in chronic lung Dx)
 - CAD
 - Nocturnal cardiac arrhythmias
 - Sudden death
- **Treatment reduces systemic HTN**
- **Treatment may reduce**
 - Pulmonary HTN
 - Cardiac events
 - Stroke recurrence
 - Mortality

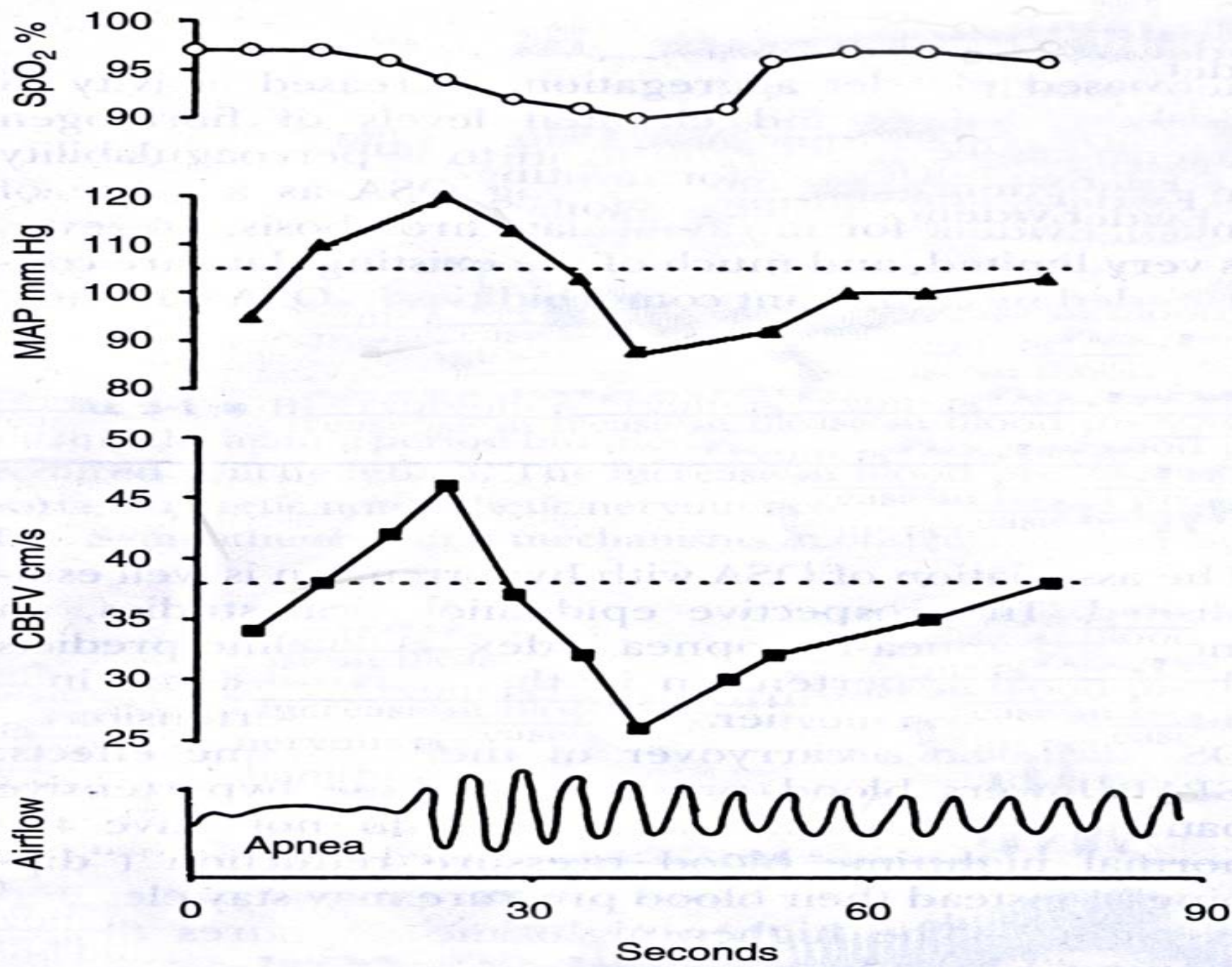


Normal



Chronic heart failure





Indication for Sleep Testing

- Nocturnal cardiac arrhythmias
- Nocturnal angina
- Difficult-to-control HTN

RECOMMENDATIONS

- HTN,
 - Pulm. HTN
 - CAD
- SHOULD PROMPT LOOKING
FOR
“Other Evidence” of OSA

Obstructive Sleep Apnea[†]: Implications for Cardiac and Vascular Disease

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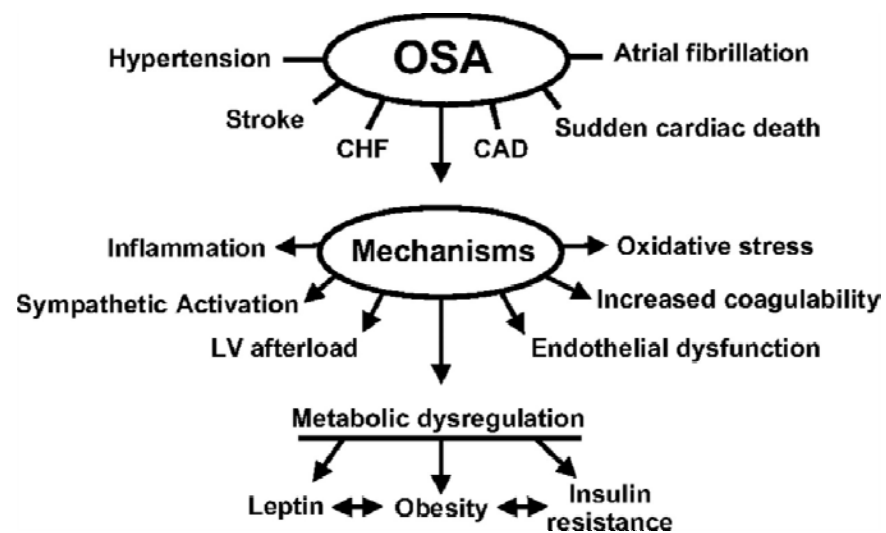


Figure Legend:

Association between OSA and cardiovascular disease; partial list of the disease mechanisms associated with OSA considered as possible links to several cardiovascular diseases and metabolic dysregulation. CHF = congestive heart failure; CAD = coronary artery disease; LV = left ventricular.