Cardiovascular Risks of OSA: Why and When to Treat

Albert A. Rizzo, MD FCCP FACP
Section Chief Pulmonary/Critical Care Medicine
Christiana Care Health System  Newark, DE
August, 2014
Sleep Apnea
Obstructive Sleep Apnea
Presentation Outline

• Epidemiology and Definition
• Pathophysiology
• The relationship to cardiovascular disease
• Diagnosis
• Treatment Modalities
Prevalence of Sleep Apnea

30-60 year olds

- **AHI > 5**
- **SAS**
- **Asthma**

Percent of Population: 0, 5, 10, 15, 20, 25

- **Male**
- **Female**
- **U.S. Pop**

The Obesity Epidemic

Adult Obesity Rate by OECD Nation, 2009

- U.S.: 33.8%
- Mexico: 30%
- Australia: 24.6%
- U.K.: 23%
- OECD Avg.: 16.9%
- Spain: 16%
- Germany: 14.7%
- Sweden: 11.2%
- Japan: 3.9%
The Obesity Epidemic

2011 Obesity Rates

- Yellow: < 25%
- Light Orange: ≥25% and <30%
- Dark Orange: ≥30%
The issue

• Obstructive sleep apnea is characterized by recurrent collapse of the upper airway during sleep resulting in intermittent hypoxia and frequent arousals.

• OSA is associated with cardiovascular morbidity and mortality
**Figure 1.** A sagittal section of a normal pharyngeal airway with the major variables contributing to airway patency/collapse shown. Reprinted by permission from Reference 2.


DOI: 10.1164/rccm.200412-1631SO
© 2005 The American Thoracic Society

One PowerPoint slide of each figure may be downloaded and used for educational not promotional purposes by an author for slide presentations only. The ATS citation line must appear in at least 10-point type on all figures in all presentations. Pharmaceutical and Medical Education companies must request permission to download and use slides, and authors and/or publishing companies using the slides for new article creations for books or journals must apply for permission. For permission requests, please contact the Publisher at dgern@thoracic.org or 212-315-6441.
Upper Airway Patency

- $P_{tm} = P_I - P_{ti}$
  - Increased $P_{tm} = \text{increased area of airway}$
  - Decreased $P_{tm} = \text{decreased area of airway}$

- Patency is determined by a balance between the action of the upper airway dilator muscles and negative intraluminal pressure.
Figure 2. A schematic representation of the interaction between soft tissue and the upper airway bony enclosure and their combined affect on airway size. Reprinted by permission from Reference 14.


Published in: David P. White; Am J Respir Crit Care Med 2005, 172, 1363-1370.
DOI: 10.1164/rccm.200412-1631SO
© 2005 The American Thoracic Society

One PowerPoint slide of each figure may be downloaded and used for educational not promotional purposes by an author for slide presentations only. The ATS citation line must appear in at least 10-point type on all figures in all presentations. Pharmaceutical and Medical Education companies must request permission to download and use slides, and authors and/or publishing companies using the slides for new article creations for books or journals must apply for permission. For permission requests, please contact the Publisher at dgern@thoracic.org or 212-315-6441.
Figure 1. Obesity and the modulation of upper airway collapsibility and sleep apnea susceptibility. Upper airway collapsibility during sleep is represented by the critical pressure ($P_{\text{crit}}$), which spans a range from health (negative) to disease (positive). $P_{\text{crit}}$ is determined by the mechanical loads imposed by boney structures and soft tissues on the pharynx, and are offset by neuromuscular responses to airway obstruction. Obesity can influence passive mechanical loads and neuromuscular control, thereby modulating upper airway collapsibility and sleep apnea susceptibility. See text for details.


Published in: Alan R. Schwartz; Susheel P. Patil; Alison M. Laffan; Vsevolod Polotsky; Hartmut Schneider; Philip L. Smith; Proc Am Thorac Soc 2008, 5, 185-192.
© 2008 The American Thoracic Society

One PowerPoint slide of each figure may be downloaded and used for educational not promotional purposes by an author for slide presentations only. The ATS citation line must appear in at least 10-point type on all figures in all presentations. Pharmaceutical and Medical Education companies must request permission to download and use slides, and authors and/or publishing companies using the slides for new article creations for books or journals must apply for permission. For permission requests, please contact the Publisher at dgern@thoracic.org or 212-315-6441.
Clinical Consequences

Sleep Apnea

Sleep fragmentation, Hypoxia / Hypercapnia

Excessive daytime sleepiness

Cardiovascular Complications

Morbidity, Mortality
Figure 2. Mechanisms associated with intermittent hypoxia/sleep fragmentation in obstructive sleep apnea contributing to cardiovascular diseases. The intermittent hypoxia and sleep fragmentation associated with obstructive sleep apnea syndrome (OSAS) result in a variety of responses, including increased sympathetic nervous system activity, systemic inflammation, oxidative stress, and metabolic dysregulation, the latter involving insulin resistance and disordered lipid metabolism. Inflammation and oxidative stress produce endothelial dysfunction, and the various mechanisms combine to promote the development of atherosclerosis and cardiovascular disease.


Published in: Walter T. McNicholas; Am J Respir Crit Care Med 2009, 180, 692-700.
DOI: 10.1164/rccm.200903-0347PP
© 2009 The American Thoracic Society
The Associations with OSA

- Hypertension
- CAD
- Stroke
- Heart Failure
- Atrial fibrillation
- Metabolic Syndrome
Mechanisms for OSA to interact with Cardiovascular Diseases and the Metabolic Syndrome

- Increased pro-inflammatory cytokines and C-reactive protein
- Higher leptin and chemerin levels in OSA
- Lower levels of adiponectin in OSA
- Effects on Fatty Acid Binding proteins
- Effects on VEGF and sCD40 may promote atherosclerosis
- Atherosclerosis, arterial stiffness, correlations with pulse wave velocity
- Reactive oxygen species, increased levels of adhesion molecules and coagulation factors
Mechanisms of Cardiovascular Complications

- Increased sympathetic activity
- Oxidative stress
- Systemic inflammation
- Insulin resistance
- Endothelial dysfunction
- Dysregulation of lipid metabolism and dyslipidemias and potential mediator of accelerated atherogenesis
Figure 1. Possible mechanistic links between obstructive sleep apnea, metabolic syndrome, and type 2 diabetes.


© 2008 The American Thoracic Society

One PowerPoint slide of each figure may be downloaded and used for educational and promotional purposes by an author for slide presentations only. The ATS citation line must appear in at least 10-point type on all figures in all presentations. Pharmaceutical and Medical Education companies must request permission to download and use slides, and authors and/or publishing companies using the slides for new article creations for books or journals must apply for permission. For permission requests, please contact the Publisher at dgerr@thoracic.org or 212-315-6441.
Figure 1. Effects of chronic intermittent hypoxia (CIH) on lipoprotein clearance. CIH inhibits triglyceride-rich lipoprotein clearance (chylomicrons [CM] and very-low-density lipoprotein [VLDL]) by activating angiopoietin-like protein-4 (Angptl-4), a potent inhibitor of lipoprotein lipase (LpL) in the adipose tissue. The decrease in the LpL activity, an enzyme that is anchored at the capillary endothelium, promotes a significant decrease in the hydrolysis of triglycerides into free fatty acids from CM and VLDL particles. The consequence of the LpL inhibition is the prolonged circulation of CM and VLDL in the bloodstream that may favor the progression of atherosclerosis.


Published in: Luciano Drager; Vsevolod Polotsky; Am J Respir Crit Care Med. 2011, 184, 288-290.
DOI: 10.1164/rccm.201105-0837ED
Copyright © 2011 American Thoracic Society
Diagnosis: History

- Snoring
- Nocturnal gasping and choking
  - Ask bed partner (witnessed apneas)
- Automobile or work related accidents
- Personality changes or cognitive problems
- Mood disturbances
- Fatigue/non-refreshing sleep
- Excessive daytime sleepiness (Epworth, Berlin, Stanford)
STOP BANG

- Snoring
- Tired
- Observed apnea
- High Blood Pressure
- BMI over 35
- Age over 50
- Neck circumference > 17 in m, 16 in f
- Gender male
- Score 3 or more yes’s = high risk
Sleep Apnea Risk Factors

- Obesity
- Increasing age
- Male gender
- Anatomic abnormalities of upper airway
- Family history
- Alcohol or sedative use
- Smoking
- Associated conditions
Associated Conditions at High-Risk for OSA

- Obesity
- CHF
- Atrial fibrillation
- Refractory hypertension
- Type 2 Diabetes
- CVA
- Nocturnal dysrhythmias
- Pulmonary hypertension
- High risk driving populations (commercial truckers)
- Pre-op Bariatric Surgery
Diagnosis: Physical Examination

- BMI > 32
- Upper body obesity / thick neck
  - ≥ 17” males, ≥ 16” females
- Macroglossia
- Mallampati Score
- Obvious airway abnormality
Exam: Tonsillar Hypertrophy

Physical Examination

Mallampati Classification

Class I

Class II

Class III

Class IV
Consequences: Cognitive and Neurobehavioral Deficits

- Cognition
- Memory
- Sustained attention/vigilance
- Divided attention
- Executive functioning
Consequences: Excessive Daytime Sleepiness

- Increased motor vehicle crashes
- Increased work-related accidents
- Poor job performance
- Depression
- Family discord
- Decreased quality of life
Consequences: Cardiovascular

- Systemic hypertension
- Cardiac arrhythmias
- Myocardial ischemia
- Cerebrovascular disease
- Pulmonary hypertension / cor pulmonale
Consequences: Metabolic

• Glucose intolerance
• Insulin resistance
• Type II diabetes mellitus
What Test Should be Used?

• In-laboratory, attended full night polysomnography
  – Split night studies

• Home diagnostic systems
  – Sleep, Cardiovascular, Oximetry, Position, Effort, Respiratory
  – High pre-test probability
Figure 1. A 30-s episode of obstructive apnea occurring during REM sleep is demonstrated. Note the increasing ventilatory effort across the episode indicating its obstructive nature. Also note the sequelae of the episode: arousal from sleep and intermittent hypoxia.

Proc Am Thorac Soc,

© 2006 The American Thoracic Society

One PowerPoint slide of each figure may be downloaded and used for educational not promotional purposes by an author for slide presentations only. The ATS citation line must appear in at least 10-point type on all figures in all presentations. Pharmaceutical and Medical Education companies must request permission to download and use slides, and authors and/or publishing companies using the slides for new article creations for books or journals must apply for permission. For permission requests, please contact the Publisher at dgern@thoracic.org or 212-315-6441.
Measures of Sleep Apnea Frequency

- Apnea = cessation of airflow for at least 10 secs
- Hypopnea = abnormal resp event lasting at least 10 secs associated with a 30% reduction in thoracoabdominal movement or airflow compared to baseline and at least 4% decrease in O2 saturation
  - Apnea Index = # apneas per hour of sleep
  - Apnea / Hypopnea Index (AHI)= # apneas + hypopneas per hour of sleep
  - AHI < 5, normal, 5-15 mild, 15-30 moderate, > 30 severe
- Respiratory disturbance index (RDI) = AHI for Medicare;
  - For others, RDI = # apneas + hypopneas + RERA’s per hour of sleep
CMS coverage for CPAP

- AHI > 15 events/hr with a minimum of 30
- AHI > 5 and < 14 events/hr with any of the following
  - Hypertension
  - History of Stroke
  - Ischemic Heart Disease
  - Excessive Daytime Sleepiness
  - Impaired cognition
  - Insomnia
  - Mood disorders
Treatment Goals

• Reduce mortality and morbidity

• Improve quality of life

• The challenge is that not all patients appreciate both goals when confronted with options for treatment vs non-treatment
Therapeutic Approach

• Risk counseling
  – Motor vehicle crashes
  – Job-related hazards
  – Judgment impairment
  – Cardiovascular risks in increased MI, CVA, death

• Treatment Modalities
  – Behavioral
  – PAP
  – Oral Appliances
  – Surgical
  – Adjuncts
Behavioral Interventions

• Encourage patients to:
  – Lose weight (15% : 30% ???)
  – Avoid alcohol and sedatives
  – Avoid sleep deprivation
  – Avoid supine sleep position
  – Stop smoking
Figure 2. Positional obstructive sleep apnea. Polysomnogram showing obstructive apneas and hypopneas occurring only during periods of supine sleep. Abbreviations for sleep stages: R = REM sleep; W = awake; 1 = stage 1 non-REM sleep; 2 = stage 2 non-REM sleep; 3 = stage 3 non-REM sleep; 4 = stage 4 non-REM sleep. Abbreviations for body position: F = front; B = back; L = left; R = right.


© 2008 The American Thoracic Society

One PowerPoint slide of each figure may be downloaded and used for educational not promotional purposes by an author for slide presentations only. The ATS citation line must appear in at least 10-point type on all figures in all presentations. Pharmaceutical and Medical Education companies must request permission to download and use slides, and authors and/or publishing companies using the slides for new article creations for books or journals must apply for permission. For permission requests, please contact the Publisher at dgern@thoracic.org or 212-315-6441.
Positive Airway Pressure
Positive Airway Pressure: Problems
Adverse Effects of PAP

• Nasal
  – Rhinorrhea, nasal congestion, oronasal dryness, epistaxis
• Mask
  – Skin abrasion/rash, conjunctivitis from air leak
• Noise
• Flow related: chest discomfort; aerophagia; sinus discomfort; claustrophobia; difficulty exhaling; barotrauma
• Partner intolerance/inconvenience
CPAP Compliance

- Patient report: 75%
- Objectively measured use
  - > 4 hrs for > 5 nights / week: 46%
- Asthma medicine compliance: 30%
- Medicare compliance = > 4 hrs, > 70% of the nights during a 30 day consecutive period
Strategies to Improve Compliance

- EDUCATION (pre, post, throughout)
- Machine-patient interfaces
  - Masks
  - Nasal pillows
  - Chin straps
- Humidifiers
- Ramp
- Desensitization
- Bi-level pressure
Oral Appliance: Mechanics
Oral Appliances

• Efficacy
  – Variable; may cure mild disease and can reduce AHI by 30-50% in more severe disease

• Side effects
  – TMJ discomfort, dental misalignment, and salivation
Uvulopalatopharyngoplasty (UPPP)
Staged Surgical Procedures
Treatment Adjuncts

- **Supplemental O2**
  - Not a primary therapy; reduces hypoxia during apneas
  - May prolong apneas
  - May reduce arrhythmias

- **Pharmacologic**
  - Modafinil/Armodafinil
  - Nasal steroids/antihistamines

- **Nasal Valves**

- **Hypoglossal nerve stimulation**
Chronic Care Management

• Risk counseling

• Behavior modification

• Monitor symptoms and compliance
  – Monitor weight and blood pressure
  – Ask about recurrence of symptoms
  – Evaluate CPAP use and side effects

Obstructive Sleep Apnea
Presentation Summary

• Epidemiology and Definition
  – 2-5% of the population; recurrent collapsibility of the upper airway during sleep leading to intermittent hypoxia and arousals

• Pathophysiology
  – The intermittent hypoxia, intra-thoracic pressure swings result in increased sympathetic activity and alteration in inflammatory processes and lipid metabolism.

• The relationship to cardiovascular disease and the metabolic syndrome
  – Association exists with increased cardiovascular events include MI’s, CVA’s, refractory hypertension and dysrhythmias.

• Diagnosis
  – Home sleep testing in those with high predictive positivity
  – In-lab study in the presence of co-morbidities.

• Treatment Modalities
  – CPAP as a first line approach coupled with behavioral modifications. Oral appliances are increasing in popularity. New advances include neuro-stimulation of oropharyngeal muscles. Surgery is less popular.
Why and When to Treat?

Take Home Message

• OSA is a common, under-diagnosed despite being easily diagnosed and treatable disease that leads to increased cardiovascular events when under-appreciated and untreated.

• The history and physical can identify risk factors for OSA. The presence and severity of OSA requires testing either in the home setting or in the sleep lab.

• Treatment should be pursued in all identified patients and includes CPAP as a first line choice and will require education of the patient and persistent efforts to improve compliance with CPAP or seek alternative treatments.
Questions?

Thank You