Obstructive Sleep Apnea and Cardiovascular Disease

Ola Akinboboye MD MPH MBA FACC

• Associate Professor of Clinical Medicine
  Cornell University
DISCLOSURE

No financial relationships but I AM PASSIONATE ABOUT THIS disease!!

Some slides were loaned to me By Dr Weisfogel
Sleep Apnea And Race

- Blacks:
  - higher prevalence of sleep apnea
  - More severe sleep apnea on presentation
  - Lower nadir of oxygen saturation during sleep apnea episodes
  - Lower scores on Epworth Sleepiness Scale

- Sands et al Chest 2008 134: s51003
Sleep Apnea

- Obstructive: 10-second cessation or reduction in airflow during sleep with ongoing ventilatory effort.

- Central: 10-second cessation or reduction in airflow during sleep without ventilatory effort.
Sleep Apnea

- Apnea > 10 sec cessation of airflow during sleep.

- Hypopnea >10sec reduction (but not cessation) in airflow associated with desaturation or arousal
Apnea-Hypopnea Index

- Total number of apneas and hypopneas per hour of sleep
  - 5-15 = Mild
  - 15-30 = Moderate
  - >30 = Severe
AHI AND RDI LIMITS REDEFINED

NEW CMS GUIDELINES FOR CPAP:

OSA EQUALS AHI OR RDI = 15 OR MORE

OR

AHI OR RDI FROM 5-14 WITH SYMPTOMS OF excessive daytime sleepiness, IMPAIRED COGNITION, INSOMNIA, HYPERTENSION, IHD, OR CVA HX
Relationship Between Obstructive Sleep Apnea and Cardiovascular Disease
LONG TERM CV OUTCOMES IN MEN WITH OSA

10 YEAR OBSERVATIONAL STUDY.

OSA Vs Normal subjects
Fatal CVD : 2.87X
Non-Fatal CVD : 3.17X

MARIN LANCET;2005:365, 1046-53
18 year follow up of 1522 middle aged patients ages 30-60

All cause mortality- 2-3 times greater in those with OSA vs. no OSA

Cardiovascular mortality- 5 to 6 times greater with OSA vs. no OSA

Sleep 2008;31(8):1071-8
DON’T GO TO SLEEP----

PEOPLE TEND TO DIE THERE

Mark Twain
Day Night Pattern of Sudden Death in OSA

- Midnight to 6AM

- OSA patients 46%
- No OSA 21%

Sert Kuniyoshi, F. H. et al. J Am Coll Cardiol 2008;52:343-346
8-h Periods of MI Occurrence

Sert Kuniyoshi, F. H. et al. J Am Coll Cardiol 2008;52:343-346
Impact of SDB on Life Threatening Arrhythmia in HF Pts with AICDs

- 71 pts with HF and ICD studied for 180 days after a sleep study (all with EF<35%)
- 66% had SDB
- Appropriate shocks in 43% with SDB vs 17% without SDB
- Shocks from 12 AM to 6 AM in 34% of SDB vs 17% without SDB

Thus SDB in pts with HF and ICDs is an independent predictor of life threatening arrhythmia more likely to occur during sleep

Serizawa et al, JACC, 10/15/08
• Pts with OSA have 3-6 X likelihood of fatal and non fatal CV events in 10-18 years and 2-3 X all cause mortality vs those without OSA.

• Pts with OSA have AICD shocks during the night, MIs during the night and die during the night. Not the case with non OSA pts.
Obstructive Sleep Apnea

What is the link between OSA and CVD?
Cardiovascular Disease
Mechanisms in Sleep Apnea

Hemodynamic Mechanism
Neurohormonal Mechanisms
Inflammatory Mechanisms
TAKE HOME MESSAGE

IN OSA PATIENTS

- R-R interval decreases
- R-R variability decreases
- BP variability increases

ALL 3 predispose to the development of cardiovascular disease (Framingham data)
Intrathoracic Pressure Changes

- Increases transmural gradients across the atria, ventricles, and aorta
- Consequences: increased wall stress, increased atrial size, impaired diastolic function, thoracic aortic dilatation/anuersym, aortic dissection
Circulating NO suppressed in OSA and reversed by CPAP

Humoral Responses to OSA
Endothelin-1

MAP (mm Hg)

ET-1 (pg/mL)

2200 H
Prior to sleep

0200 H
Awake before CPAP

0700 H
Awake after CPAP

P<0.05

P<0.001

P<0.03

P<0.05

Phillips BG et al: J Hypertens 17:61, 1999
Increased CRP in Patients with OSA

P < 0.0003

Shamsuzzaman et al: Circulation, 2002
Effect of nCPAP (1 month) on CRP and IL-6 levels

Yokoe et al, Circulation 2003
OSA and Risk of Incident AF


- 3542 consecutive Olmsted County adults
  - No current AF or past history of AF
  - First diagnostic polysomnography

- Follow-up to December 2003 for 1st AF (or flutter)
  - Censored at death, last follow-up date, or AF
  - Mean follow-up: 5 years (maximum: 16 years)

Incidence of AF by OSA Status

\[ P = 0.002 \]

PRESIDENT WILLIAM H. TAFT

- YALE UNIVERSITY, CINCINNATI LAW SCHOOL
- GOVERNOR OF THE PHILIPPINES 1900-1903
- SECRETARY OF WAR 1907
- PRESIDENT OF THE UNITED STATES 1909-1913
- CHIEF JUSTICE OF THE SUPREME COURT 1921-1930
C-Reactive Protein

- found within atheromatous plaque
- correlates with vascular dysfunction
- promotes secretion of inflammatory mediators
- promotes cell adhesion molecule expression
- opsonizes LDL for uptake by macrophages in atherosclerotic plaque
Relative risk of a first MI associated with baseline CRP, stratified according to aspirin or placebo therapy (the Physicians' Health Study)

![Bar chart showing the relative risk of myocardial infarction by quartile of plasma C-reactive protein levels with aspirin and placebo.](chart)

Anecdotes About President Taft and Sleep Apnea

- 1900: Reportedly slept through a thunderous and terrifying typhoon in the Philippines
- His wife and staff had to devise creative techniques to keep him wake during state functions
- Dropped his weight from 340 to 264 pounds
- Returned as Chief Justice of the Supreme Court in 1921.
Obstructive Sleep Apnea

- “I was nervous and fretful and for a month I found it hard to sleep”
  
  - William Taft
Sleep Apnea – The Future State?

- Screening
  - Cardiologist
- Monitoring
  - Cardiologist
  - Cardiologist and/or Sleep Specialist
- Diagnosis
  - Cardiologist
- Treatment
Who Should Be Screened for OSA

- Patients with
  - Hypertension
  - Atrial Fibrillation
  - Congestive Heart Failure
  - Excessive daytime somnolence
  - Stroke
  - Coronary Artery Disease
  - Insulin Resistance
  - Obesity
Baseline: 150 - 0 = 150
Phenylephrine: 200 - 0 = 200
OSA: 150 - (-50) = 200
Cardiovascular Disease Mechanisms in Sleep Apnea

- Introduction
- Neural mechanisms
- Vascular mechanisms
- Inflammation
- Summary
How To Screen

1) When do you go to bed at night?
2) When do you wake-up?
3) Are you sleepy? (Epworth sleepiness scale)
OSA and AF: Recurrence

- Controls: 53%
- Untreated OSA: 82%
- Treated OSA: 42%

Epworth Sleepiness Scale

Sitting and reading

Watching TV

Sitting inactive in a public place

Being a passenger in a motor vehicle for an hour or more

Lying down in the afternoon

Sitting and talking to someone

Sitting quietly after lunch (no alcohol)

Stopped for a few minutes in traffic while driving
Cardiovascular Conditions That Are Affected by OSA

- Hypertension
- Atrial Fibrillation
- Other Arrhythmias
- Congestive Heart Failure
- Stroke
- CAD
SLEEP - A NEW CARDIOVASCULAR FRONTIER

V.K. SOMERS
MAYO CLINIC
Cardiovascular Disease Mechanisms in Sleep Apnea

- Introduction
- Neural mechanisms
- Vascular mechanisms
- Inflammation
- Summary
Awake

[Graph showing physiological signals labeled as 'NORMAL' and 'OSA' in the awake state.]

Somers et al, JCI
Control Subject

- ECG
- HR 64 beats/min

Severe OSA Patient

- ECG
- HR 82 beats/min
- BP (mm Hg)
- Neurogram
- Respiration

Narkiewicz et al: Circulation, 1998
• CPAP attenuates sympathetic activation in patients with OSA and optimally treated CHF (beta blockers, ACEI etc.)

IMPLICATION: Untreated OSA in such patients may be as harmful as suboptimal treatment with beta blockers!
Cardiovascular Disease Mechanisms in Sleep Apnea

- Introduction
- Neural mechanisms
- Vascular mechanisms
- Inflammation
- Summary
Endothelium

PreProET → ET-1

ET₁

NOS III

BH₄

ET₂

ECE

NO

VSM

Contraction

Relaxation
Resistance Vessel Function in OSA Impairment of Endothelium Mediated Vasodilation

Causes and effects of endothelial dysfunction

Traditional Risk Factors

Non-traditional Risk Factors

Local Factors

Genetic Predisposition

Unknown Factors

Endothelial Dysfunction: "The Risk of the Risk Factors"

Vascular Lesion and Remodeling

Inflammation

Vasoconstriction

Thrombosis

Plaque Rupture/Erosion

Lerman, A. et al. ATVB. 2003
Cardiovascular Disease Mechanisms in Sleep Apnea

- Introduction
- Neural mechanisms
- Vascular mechanisms
- Inflammation
- Summary
Comparison of CRP to other lipid and non-lipid risk factors for cardiovascular disease

Ridker, Circulation 2003
Circulating IL-6 at 4559 m

Hartmann et al: Cytokine, 1999
Circulating CRP at 4559 m

Hartmann et al: Cytokine, 1999
Effects of Statin Therapy on CRP Levels

N=22

P, pravastatin
S, simvastatin
A, atorvastatin

Hs-CRP (mg/L)

Baseline P S A
(40 mg/day) (20 mg/day) (10 mg/day)

Jialal et al. (Circulation, 2001)
Eugene Braunwald—2001 Shattuck Lecture

- There are 2 emerging epidemics:
  - Atrial fibrillation
  - Heart failure

OSA and AF: Prevalence

- Methods:
  - 524 consecutive patients
    - 151 with AF from Mayo Clinic Cardioversion Center
    - 373 from a general cardiology practice
  - Prospective assessment of OSA
    - Berlin questionnaire
    - Validation series with full sleep studies

Untreated OSA With and Without Recurrence

% Fall in Nocturnal Oxygen Saturation

- No Recurrence: 8%
- Recurrence: 22%

\[ P = 0.034 \]

% Nights with Nocturnal Oxygen Saturation < 90%

- No Recurrence: 15%
- Recurrence: 30%

\[ P = 0.063 \]

CRP IN HEART FAILURE

- CRP LEVELS AT ACUTE HEART FAILURE ADMISSION PREDICTS LONG TERM MORTALITY

Central Sleep Apnea and Heart Failure

Hypersomnolence → Fatigue

Sleep Disruption

Pulmonary edema

Pulmonary afferent stimulation

Left Ventricular Failure:
- Cardiac Output
- LV Filling Pressure

Arousal

Hyperventilation

PaCO₂

Central Apnea

PaO₂

SNA
- Catecholamines
- HR

Cardiac O₂ Supply vs. Demand

Bradley, Floras, Journal of Cardiac Failure, 2:223-240
Acronym for OSA and CHF

- A----
- O----
- O----
- E----
Acronym for OSA and CHF

- A---- AFTERLOAD
- O---- OVERLOAD
- O---- OVERNIGHT
- E---- EVERYNIGHT
Effect on CHF volume overload

- Initiation of Auto titrating CPAP: pressure 18 cm
- Daily weight monitoring – no change in diuretic medication
- Download of CPAP data: pressure dropped to 8 cm

Data on file: Dr. Randall Williams, Northwestern University
Prevalence of sleep apnea in patients with CHF

- Javaheri 1998
- Chan 1997
- Sin 1999

n=81, n=20, n=450
...Prevalence of SDB in CHF patients treated with Beta Blockers

Macdonald et al, Journal of Clinical Sleep Medicine 2/2008
Heart Failure Patients

108 Consecutive

SDB in 61%

CSR in 31%

OSA in 30%
## Difference between Groups with and without SDB

<table>
<thead>
<tr>
<th></th>
<th>Atrial Fibrillation</th>
</tr>
</thead>
<tbody>
<tr>
<td>SDB</td>
<td>21%</td>
</tr>
<tr>
<td>No SDB</td>
<td>2%</td>
</tr>
</tbody>
</table>
Differences between CSR and OSA groups

<table>
<thead>
<tr>
<th></th>
<th>CSR</th>
<th>OSA</th>
</tr>
</thead>
<tbody>
<tr>
<td>NYHA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Class II</td>
<td>44%</td>
<td>70%</td>
</tr>
<tr>
<td>Class III-IV</td>
<td>56%</td>
<td>30%</td>
</tr>
<tr>
<td>LVEF%</td>
<td>15%</td>
<td>24%</td>
</tr>
<tr>
<td>A-Fib</td>
<td>28%</td>
<td>8%</td>
</tr>
</tbody>
</table>
218 Patients in HF Clinic 1997-2005

- 117 (54%) Mild or No OSA
- 56 (26%) OSA
- 45 (21%) CSA
56 OSA Patients

41 Untreated
4 Lost to FU

15 Treated
1 Lost to Follow up
Mortality Rates (mean 2.9 years)

- 1. Mild or No OSA 12%
- 2. Untreated OSA 24%
- 3. Treated OSA 0%
Sleep Monitoring at CHF Clinic

MD, NP, or PA Assessment with Sleep questionnaire

Smart Card monitoring

Watch PAT
Cardiovascular Disease Mechanisms in Sleep Apnea

- Introduction
- Neural mechanisms
- Vascular mechanisms
- Inflammation
- Summary
As I gazed at him, knowing him to be Brahms, I was utterly unable to recognize the man I had known ten years previously. There, indeed, was the great head with the hair brushed back as of old, though less tidily than in former days; but his figure had become much heavier, and both mouth and chin were hidden by a thick moustache and shaggy, grizzled beard that had completely transformed his appearance.

Florence May 1881
Johannes Brahms (1833-97)

- One of 3 great “B” composers (Bach, Beethoven, Brahms)
- Never married- although deeply loved Robert Schumann’s wife Clara
- His traveling companion insisted on separate rooms because he snored loudly
- Never wore neckties because neck was so large
- Was irritable and nasty- “If there is anyone here I have not offended, I apologize”
Disclosures

• Medical Director Healthy Heart Sleep

• Speaker for Respironics
1. Any combination of two or more of the following symptoms of sleep apnea {a. through e.}:

A. Excessive daytime sleepiness as evidenced by inappropriate daytime napping (e.g., during driving, conversation, or eating); sleepiness that interferes with daily activities or an Epworth Sleepiness Scale score greater than 10; or

B. Persistent or frequent socially disruptive snoring or choking or gasping episodes associated with awakenings; or

C. Obesity (BMI greater than 30 kg/m²); or

D. Unexplained hypertension; or

E. Craniofacial or upper airway soft tissue abnormalities
2. Nocturnal oxygen desaturation with unexplained right heart failure, cardiac arrhythmias during sleep or pulmonary hypertension.; OR

3. Individuals with moderate or severe congestive heart failure, stroke/TIA, coronary artery disease, or significant arrhythmias who have nocturnal symptoms suggestive of a sleep related breathing disorder or otherwise suspected of having sleep apnea.