Sleep and the Heart

- Overview of sleep
- Hypertension
- Arrhythmias
- Ischemic events
- CHF
- Pulmonary Hypertension
- Cardiac Meds and Sleep

Sleep Stages

- Non-REM sleep (75-80%)
  - Stage 1 (5%)
  - Stage 2 (50%)
  - Stage 3-4 (15-20%)
- REM sleep (20-25%)

  (*3/4 sleep = slow wave sleep = delta sleep)

Sleep and the Heart: non REM

- Stage 1
  - Stable autonomic regulation
  - Marked sinus arrhythmia
- Stage 2
  - Bursts of sympathetic activity - K Complexes
  - Increased HR and BP
- Stage 3-4 (SWS)
  - Decline in muscle sympathetic activity
  - Slow HR and low BP
  - A very stable state
Sleep and the Heart: REM

- REM
  - Increased Sympathetic Activity
  - Variable HR and BP
  - Sinus arrest at REM onset

Overall Cardiovascular Response to Normal Sleep

- Fall in epinephrine
- Fall in heart rate
- Fall in morning BP (morning dip)
- Fall in cortisol (until 5 a.m.)
- Sympathetic activity declines
- Overall arrhythmogenicity falls

Recumbency

- Lying down increases cardiac filling pressures
  - Increased sympathetic activation
- Lying down increases upper airway edema in patients with CHF
  - Worsens pre-existing SDB
Sleep-Disordered Breathing
A Brief Review

- New definitions (CMS, AASM SHHS 2001)
  - Apnea:
    - 90% reduction in airflow for 10 seconds
  - Hypopnea
    - 30% reduction in airflow with 4% desat for 10 sec
  - Obstructive sleep apnea hypopnea syndrome (OSAHS=SDB=OSA)
    - AHI=RDI greater than or equal to 5 with symptoms

Sleep-Disordered Breathing and Hypertension

- Normal blood pressure and heart rate response to sleep is to decline 10% (10-20 mmHg)
  - Those who don’t are “nondippers”
  - Nondipping carries risk of
    - Ventricular arrhythmias
    - Cardiac hypertrophy
    - Sudden cardiac death (in women)
SDB and Hypertension Mechanism

- Those with higher AHI's have higher a.m. blood pressures
- SDB coverts dippers to nondippers
- Reflex activation of sympathetic nerves by hypoxemia
- Impaired baroreceptor sensitivity
- Increasing respiratory effort (pulsus paradoxus)

SDB HTN and Endothelial Dysfunction

- Endothelial Cells
  - ET-1 vasoconstriction
  - NO vasorelaxation
- SDB
  - Hypoxemia
  - ET-1
  - Increased BP
  - NO decreased = decreased vasorelaxation = increased vascular tone
  - Inflammation
    - Hypoxemia and sleep deprivation increase prod. of proinflammatory cytokines-CRP

Figure 2 - Proposed physiologic interactions between OSA, cerebrovascular risk mechanisms and overt cerebrovascular disease. In OSA, sleep-disordered breathing contributes to acute cerebrovascular insults which, over time, may promote cerebrovascular mechanisms (blue circles) that result in cerebrovascular disease (green circle). Interactions with other risk factors (orange circle) may choose individual phenotypic outcomes or the cerebrovascular response to OSA therapy.
Sleep Apnea and Hypertension: Summary

- Sleep apnea is a risk factor for HTN
- Sleep apnea is especially a risk factor for drug resistant HTN
- Effective CPAP lowers BP; ineffective CPAP does not
- In patients with OSA, effective CPAP would be expected to reduce coronary heart disease risk by 37% and stroke by 56%

Arrhythmias...a Review

- Normal sleep results in
  - Decreased sympathetic activity
  - Increased parasympathetic activity
  - Reduced heart rate
  - Reduced blood pressure
  - Slowed AV node conduction
  - Prolongation of cardiac refractory periods
  - Reduced arrhythmogenicity overall

Ventricular Arrhythmias

- Variable response to sleep in normals
- Increase in PVC's between 6 and 11 am
- V tach and V fib peak at awakening
- Beta blockade eliminates the circadian variation of sudden cardiac death and sustained VT
SDB and Arrhythmias

- Cyclical brady/tachycardia is a sensitive (95%) but not specific (48%) for OSAHS
- Sinus arrest occurs in 10% with OSAHS
- AV block occurs in 5% with OSAHS
- VT occurs in 3-13% of those with SDB
- Severe OSA, morbid obesity, severe O2 desats predict heart block, arrhythmias
- O2 and CPAP reduce arrhythmias

OSA and Ischemia: Mechanism

- C-reactive protein (CRP) is increased
  - CRP induces cell adhesion molecules
  - Risk of CVD correlates with CRP levels
  - CRP levels correlate with severity of SDB
  - CPAP lowers CRP
- Insulin resistance/metabolic syndrome risk is increased
  - Insulin resistance increases with increasing AHI, controlling for BMI

Obesity and SDB

- Reactive Oxygen Species (ROS)
  - Upregulate vascular adhesion molecules
  - Increase platelet aggregation
  - Scavenge NO
SDB and Ischemia

- OSAHS is implicated as a cause of MI
- Death is increased in those with AI>20
- Cardiac patients with high rates of SDB have far higher rates of MI
- Pathogenesis is reduced myocardial O2 due to bradycardia, asystole, and hypoxemia, increased viscosity, and platelet activation

CSA and CHF

- A consequence of HF
  - Caused by oscillations of PaCO2 around apnea threshold
- HF patients with CSA are hypocapnic
  - Pulmonary congestion
    - Stimulates vagal irritant receptors
    - Increases central & peripheral chemosensitivity
    - Causes arousals
Sleep-Disordered Breathing in Patients with NYHA 2 CHF

<table>
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<th>Author</th>
<th>n</th>
<th>Patients with SDB</th>
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<tr>
<td>Naughton</td>
<td>74</td>
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<td>Javaheri</td>
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<td>41 (51%)</td>
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<td>46 (69%)</td>
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Sleep-Disordered Breathing and CHF

- Central Sleep Apnea (CSA)
  - Present in approx 40% of CHF patients
  - Results from CHF
- Obstructive Sleep Apnea (OSA)
  - Present in 5-10% of CHF patients
  - Results in CHF

CHF and Central Sleep Apnea

- May result from increased CO2 sensitivity
- May be assoc. with increased risk of arrhythmias
- Predicts early mortality in CHF
- May be assoc. with PLM increased arousals, and disturbed sleep
- CPAP may enhance survival
CHF and Obstructive Sleep Apnea

- OSA induces high sympathetic activity
- OSA results in very strongly negative intrathoracic pressures (Mueller maneuvers)
  - Increased cardiac transmural pressure
- OSA is linked to endothelial dysfunction
  - Impaired vasodilator response
- OSA results in oxygen desaturation
  - Worsening ischemia and cardiac function

CSA and CSR

- Pulmonary Congestion
- J-Receptors in Alveolar Wall
- Hyperventilation
- Apneic Threshold and pCO2
- Chemoreceptors-Peripheral and Central
- Decreased CO and Lag Time
- Over and Undershoot

![Fig. 1. Mechanisms for initiation and perpetuation of CSR. Dioxide diffusion capacity of carbonaceous tissue.](image)
Risk Factors for SDB in Patients with CHF (Sin DD et al, 1999 n=450, 282 men)

- CSA
  - Male gender
  - Atrial fibrillation
  - Age > 60
  - Hypocarbia (PaCO2 < 38 mm Hg)

- OSA
  - In men, BMI > 35
  - In women, age > 60 years

CPAP, CSA, AND CHF (Kaneko Y, NEJM, 2003)

- CPAP improves LV function, heart rate and blood pressure in patients with heart failure and coexisting obstructive sleep apnea
- These patients were not sleepy!! (ESS approx 6)
  - The effects extend into the daytime


- N=55, 19 CPAP and 21 Control
- These patients were not sleepy (ESS-9)
- CPAP
  - Improved LV function
  - Lowered urinary norepinephrine
  - Improved quality of life
ASV Adaptive Servo Ventilation

- EEP
- PS min Hyperventilation
- PS max Hypoventilation
- Steady Resp. Rate and airflow

SDB and Pulmonary Hypertension
The Bottom Line

- Probably occurs in about 20% of patients with OSA
- More prevalent in:
  - Those with higher BMI
  - Those with lower SaO2's
  - Those who smoke
- SaO2 is a better predictor than AHI
- CPAP improves it!!

Beta Blockers and Sleep

- Compared with placebo, lipophilic beta blockers:
  - Increase REM latency, reduce REM
  - Increase W, TWT, stage 1
  - Deplete endogenous melatonin
  - Are associated with nightmares
Summary

• Sleep reduces cardiac risk in normals
• REM sleep is a vulnerable time for cardiac patients
• OSAHS causes cardiovascular disease
  – Hypertension, systemic and pulmonary
  – Ischemic events
  – Arrhythmias
  – CHF
• Beta blockers disrupt sleep, but save lives
• CPAP reduces cardiac risk of SDB

QUESTIONS

Thank you
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