Cardiovascular Consequences of Obstructive Sleep Apnea

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Increased Mortality in OSA
Wisconsin Sleep Cohort Study

Young et al. Sleep 31:1071-8, 2008

% Surviving

Years of Follow-up

Total Sample

Sample Excluding CPAP Treated Participants

AHI < 5
AHI 5-15
AHI 5-30
AHI ≥ 30

AHI < 5
AHI 5-15
AHI 5-30
AHI ≥ 30

Young et al. Sleep 31:1071-8, 2008
Day-Night Pattern of Sudden Death in Obstructive Sleep Apnea

Gami et al. NEJM 352:1206-14, 2005
Acute Hemodynamic Effects of OSA

OSA and the Pulmonary Circulation

Obstructive Apnea

↓ PaO₂  ↑ PaCO₂

Pulmonary Artery Hypertension

Cor Pulmonale

RIGHT SIDED CHF (Pickwickian)
Association of Nocturnal Arrhythmias with Sleep Disordered Breathing

- Nested group-matched exposed and non-exposed design
- Group frequency matching to obtain covariate distributions of age, sex, race/ethnicity and BMI

<table>
<thead>
<tr>
<th></th>
<th>$AHI &lt; 5\ n = 338$</th>
<th>$AHI \geq 30\ n = 228$</th>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial fibrillation</td>
<td>0.9%</td>
<td>4.8%</td>
<td>4.02</td>
<td>1.03 – 15.74</td>
</tr>
<tr>
<td>Non-sustained ventricular tach</td>
<td>1.2%</td>
<td>5.3%</td>
<td>3.40</td>
<td>1.03 – 11.20</td>
</tr>
<tr>
<td>Complex ventricular ectopy</td>
<td>14.5%</td>
<td>25.0%</td>
<td>1.74</td>
<td>1.11 – 2.74</td>
</tr>
</tbody>
</table>

*Mehra et al. AJRCCM 173:910-6, 2006*
### Association of Nocturnal Arrhythmias with Sleep Disordered Breathing

<table>
<thead>
<tr>
<th></th>
<th>$AHI &lt; 5$</th>
<th>$AHI \geq 30$</th>
<th>$p$ values</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$n = 338$</td>
<td>$n = 228$</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>68.6 ± 9.1</td>
<td>70.6 ± 9.7</td>
<td>0.01</td>
</tr>
<tr>
<td>BMI</td>
<td>30.1 ± 4.4</td>
<td>28.5 ± 4.3</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>39.7%</td>
<td>58.6%</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>50.0 ± 15.7</td>
<td>46.8 ± 13.6</td>
<td>0.02</td>
</tr>
<tr>
<td>Coronary Heart Disease</td>
<td>11.0%</td>
<td>20.2%</td>
<td>0.002</td>
</tr>
<tr>
<td>Pacemaker</td>
<td>0.9%</td>
<td>3.1%</td>
<td>0.05</td>
</tr>
</tbody>
</table>

*Mehra et al. AJRCCM 173:910-6, 2006*
Association Between SDB and Overall Cardiovascular Disease

Shahar E et al., AJRCCM 163:19-25l, 2001
OBESITY

↑ FFA

↑ Sympathetic Activity

↑ Oxidative Stress

INSULIN RESISTANCE

Glucose Intolerance

Dyslipidemia

Hypertension

Endothelial Abnormalities

Atherosclerosis

Arterial Stiffening

LV Hypertrophy

CARDIOVASCULAR DISEASE
Does Sleep Apnea Cause Hypertension, Stroke, and Cardiac Disease?
Cardiovascular Outcomes with or without CPAP Treatment

Lipid Lowering Medication Adherence

Initiation of CPAP for OSA

Medication Adherence (Exposure)

Initial CPAP Adherence (Outcome)

- 365

365 Days

0

(7 days)

- 330 patients with newly dx’ed OSA started on CPAP therapy in 2005-2006
- 142 on lipid lowering medication
- 117 with CPAP adherence data in first wk

Lipid Lowering Medication Adherence

Initiation of CPAP for OSA

Medication Adherence (Exposure)

Initial CPAP Adherence (Outcome)

- 365

365 Days

0

(7 days)

Simvastatin 20 mg/day

60

90

90

80

45

% Refill Adherence = 78%

Probability of Adequate CPAP Adherence by Medication Adherence Subgroup

Adjusted probability of CPAP use ≥ 4 hours/day*

- **“Low”** (n=60)
  - 70% (IQR 48-81)

- **“High”** (n=57)
  - 99% (IQR 96-100)

* Adjusted for age, race, AHI, Epworth, BMI, Charlson Index, first day of use.
Effect of CPAP Treatment on Mean Ambulatory Blood Pressure

Mean blood pressure (mm Hg)

- Subtherapeutic CPAP (n=59)
- Therapeutic CPAP (n=59)

Effects of CPAP Treatment on Insulin Sensitivity (ISI) are Greater in Less Obese

Harsch et al. AJRCCM 169:156-62, 2004
CPAP Treatment Decreases CRP and IL-6 Levels in Patients With OSAS

Yokoe et al., Circulation 107:1129-34, 2003
CPAP Treatment Reduces Pulse Wave Velocity in OSA Patients

Drager et al. AJRCCM 176: 706-12, 2007
CPAP Treatment Improves in LVEF Patients with Heart Failure and OSA

Mansfield et al. AJRCCM 169:361-6, 2004
Why Should OSA Patients Be Treated?

Good evidence that CPAP treatment:
• Decreases EXCESSIVE DAYTIME SLEEPINESS
• Improves QUALITY OF LIFE
• Decreases risk of MOTOR VEHICLE CRASHES
• Improves COGNITIVE FUNCTION

Does CPAP treatment:
• Reduce HYPERTENSION??
• Decrease risk of CARDIOVASCULAR DISEASE??
• Decrease risk of DIABETES MELLITUS????
Goals of this RFA are to demonstrate:

• The timely recruitment of community-based individuals at high risk for CVD

• The feasibility of long-term positive airway pressure (PAP) treatment in this participant cohort

• The potential for such treatment to produce changes in CVD risk profiles

• The minimum dose of PAP needed to show changes in intermediate markers of cardiovascular risk

• The feasibility of study design strategies for a future event driven Phase III clinical trial
Conclusions – OSA and CVD

• Sinus brady-tachy arrhythmia and atrial fibrillation are common HR abnormalities
• OSA can lead to pulmonary artery hypertension
• Evidence suggests that CPAP treatment may decrease the incidence of CVD independent of HTN and other co-morbid conditions
• CPAP treatment reduces inflammatory and oxidative stress biomarkers
• CPAP treatment reduces sympathetic tone and systemic BP
• CPAP treatment improves LV function in patients with OSA and heart failure