Sleep Apnea as a Cardiovascular Disease

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Ohio State University
Presentation Outline

- Case presentation
- Mechanism of the cardiovascular consequences of OSA
- OSA and heart failure
- SDB and heart failure: rationale for case finding
Case history

• 57 y/o school bus driver presents to the Sleep Center with:
  – Excessive daytime sleepiness
  – Snoring
  – Witnessed apnea
  – Spouse moved out of bedroom

• “Not as focused as he used to be on the job”!
Sleep History

- Seven hours of allowed sleep per night - very tired in the morning
- Awakens 3-4 times at night to use rest room
- Persistent loud snoring
- Leg jerks and kicks, restless sleep
Case History

- MHX:
  - Hypertension
  - Hypercholesterolemia

- ROS:
  - 35 lbs weight gain/past two year

- SoHx:
  - 40 Pack/year
Physical Examination

- BMI 36
- Mallampati class III, lateral peritonsillar narrowing
- Neck collar size 18 inch
- Lungs clear
- Regular rhythm- no gallop
- No edema
• **OSA - why should I care?**

• **If I have to care, what should I do about it?**

• **Treatment of OSA in patients with heart disease is a waste of time!**
### Prevalence of Obstructive Sleep Apnea

#### The Occurrence of Sleep-Disordered Breathing among Middle-Aged Adults

The Wisconsin Sleep Cohort, NEJM 1993

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>APNEA–HYPOPNEA SCORE</td>
<td>APNEA–HYPOPNEA SCORE</td>
</tr>
<tr>
<td></td>
<td>$\geq 5$</td>
<td>$\geq 10$</td>
</tr>
<tr>
<td>30–39</td>
<td>6.5 (1.4–11)</td>
<td>4.9 (0.6–9.8)</td>
</tr>
<tr>
<td>40–49</td>
<td>8.7 (4.2–13)</td>
<td>4.9 (1.7–8.1)</td>
</tr>
<tr>
<td>50–60</td>
<td>16 (5.2–26)</td>
<td>5.9 (0.0–12)</td>
</tr>
<tr>
<td>30–60*</td>
<td>9.0 (5.6–12)</td>
<td>5.0 (2.4–7.8)</td>
</tr>
</tbody>
</table>

*Values are adjusted to the age distribution of the survey population.
Overweight and obesity

Overweight including obese, 20-74 years

Overweight, but not obese, 20-74 years

Obese, 20-74 years

Overweight, 6-11 years

Overweight, 12-19 years

Year

1960-63-66-69-72-75-78-81-84-87-90-93-96-99-02-05

62 65 70 74 78 82 86 90 94 98 02 06

Percent

0 10 20 30 40 50 60 70 80 90 100

SOURCES: Centers for Disease Control and Prevention, National Center for Health Statistics, Health, United States, 2006, Figure 13. Data from the National Health and Nutrition Examination Survey.
The effects of gender and BMI change with aging.

After the age of 50, *gender* becomes an unimportant variable.

After the age of 60, *BMI* becomes an unimportant variable.

(Tishler PV, JAMA 2003)
Symptoms of OSA

- Snoring
- Excessive daytime sleepiness
- Witnessed apneas
- Poor memory and concentration, irritability or personality changes
- Other: Dry throat, morning headache, and nocturia
Sleep Apnea - Presentation in a Cardiology Practice

- Hypertension
- Left ventricular hypertrophy
- Nocturnal angina
- Myocardial infarction
- Bradyarrhythmias, ventricular arrhythmias
- Cor pulmonale
- Decompensated heart failure
Cardiovascular Consequences of Sleep Apnea
Components of the Cardiovascular response to Apnea

- Asphyxia (hypoxia-Hypercapnea)
- Increased sympathetic activity
- Blood pressure surge
- Arousal
- Respiratory Effort
Increased Negative Intrathoracic Pressure

- Increased systolic transmural pressure
- Increased LV afterload

- Increased venous return
- RV overload
- Impaired LV filling

Reduced stroke volume and cardiac output

LV systolic dysfunction

HEART FAILURE
Hypercapnea
Hypoxia

- Pulmonary vasoconstriction
  - Increased RV afterload
- Oxidative mediated endothelial dysfunction
  - Hypertension
  - CAD
  - Platelet activation
  - Myocardial ischemia

HEART FAILURE
Hypercapnea

Increased Sympathetic Activity

Endothelial damage

Decreased coronary perfusion

Increased blood pressure

Increased afterload

Myocardial ischemia

Arrhythmia

HEART FAILURE
Association Between Sleep Apnea and Incident Hypertension During 4 Year Follow Up Period

Hypertension = BP of at least 140/90 or use of anti-hypertensive medications

Peppard et al, NEJM 342:1378-1384, 2000
OSA-Induced Hypertension: Animal Model

Effect of CPAP on Blood Pressure in Hypertensive Patients

Figure 2. Changes in blood pressure with effective (closed bars) and subtherapeutic (open bars) nCPAP. *Significant difference. MAP indicates mean arterial blood pressure; systolic, systolic blood pressure; and diastolic, diastolic blood pressure. MAP, P=0.01; systolic blood pressure, P=0.04; diastolic blood pressure, P<0.005.
Hypertension and OSA

- OSA is a cause of hypertension
- Intermittent Hypoxia is the critical stimulus for the hypertensive response in patients with OSA.
- Treatment of OSA improves control of HTN
Stroke vs. AHI (Sleep Heart Health Study)
Figure 1. Kaplan–Meier Estimates of the Probability of Event-free Survival among Patients with the Obstructive Sleep Apnea Syndrome and Controls.

(Yaggi HK NEJM 2005)
OSA after stroke and the Probability of Death

(Yaggi HK NEJM 2005)
Increased incidence of coronary artery disease in sleep apnea

Peker et al Eur Resir J 2006
Increased incidence of coronary artery disease in sleep apnea

Peker et al. Eur Respir J 2006
CAD and Treatment of OSA

OSA and CAD - The Sleep Heart Health Study

OSA and CHF-the Sleep Heart Health


n=6,424
Atrial Fibrillation and OSA

• Prevalence of OSA in patients with A fib is higher than other patients of cardiology practice
• Association in Sleep Heart Health Study
• Association between OSA and recurrence of A fib following cardioversion
• Impact of OSA on atrial electromechanical activation time
  - Lim et al circ r 2009
## Association Between Severe OSA (AHI >30) and Arrhythmias in Sleep Heart Health Study

(Mehra et al, AJRCCM, doi:10.1164/rccm.200509-1442OC)

<table>
<thead>
<tr>
<th>Arrhythmia Type</th>
<th>Unadjusted Odds Ratio (95% CI)</th>
<th>Odds Ratio* (95% CI) Adjusted for Age, Sex, BMI</th>
<th>Odds Ratio* (95% CI) Adjusted for Age, Sex, BMI, CHD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-sustained ventricular tachycardia</td>
<td>4.64 (1.48-14.57)</td>
<td>3.72 (1.13-12.2)</td>
<td>3.40 (1.03-11.2)</td>
</tr>
<tr>
<td>Complex ventricular ectopy</td>
<td>1.96 (1.28-3.00)</td>
<td>1.81 (1.16-2.84)</td>
<td>1.74 (1.11-2.74)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>5.66 (1.56-20.52)</td>
<td>3.85 (1.00-14.93)</td>
<td>4.02 (1.03-15.74)</td>
</tr>
</tbody>
</table>

BMI=body mass index; CHD=coronary heart disease

*Results of logistic regression analysis with SDB as the exposure; N=338 without SDB, N=228 with SDB
Sudden Cardiac Death in OSA

OSA and Cardiovascular Disease

- OSA is present in at least 10-25% of patients 30-60 years old.
- Prevalence increases with obesity and aging—both risk factors for heart failure.
- OSA is a cause of hypertension and a risk factor for CAD, the most common causes of heart failure.
- OSA is present in up to 60% of patients with heart failure.

Adams et al (ADHERE) Am Heart J, 2005
Niemenen (EHFS II) Eur Heart J, 2006
Khayat 2009, Pauline 2009
Causative Role of Severe Untreated OSA in Cardiovascular Events
(Marin et al, Lancet 365:1046, 2005)
OSA is a Cardiovascular Risk Factor

- OSA is a cardiovascular risk factor just like high cholesterol and diabetes
  - Certain cardiovascular risk factors are modifiable
  - Early identification and treatment of cardiovascular risk factors is the current focus of care
  - Treatment of co-existent OSA in patients with established heart disease is critical
C-Reactive Protein is Increased in Moderate to Severe Sleep Apnea
A) FMD of brachial artery in 14 subjects with OSA at baseline and after 4 weeks of (n CPAP) (p = 0.001).

B) FMD of brachial artery in 13 subjects with OSA at baseline and after 4 weeks of observation (p = 0.12).
Effects of OSA on Atherosclerosis

Drager et al AJRCC 2005
Change in Glucose with CPAP

Change in HbA1c with CPAP

(Babu Arch Intern Med 2005)
Hypoxia

Increased Negative Intrathoracic Pressure

Hypoxia

Increased Sympathetic Activity

HEART FAILURE

• Pulmonary edema
  • Increased circulatory delay
  • Hyperventilation
  • Decreased cerebral blood flow

Upper airway resistance

OSA

CSA
CPAP improves LVEF in patients with CHF

OSA- Presentation in Heart Failure

OSA- Presentation in Heart Failure

Epworth Sleepiness Scale (ESS) score and sleep structure by apnea-hypopnea index (AHI) categories (<5, 5-14, and ≥15)

Mechanism of OSA in Heart Failure

Fluid Shift and Pharyngeal Resistance in Healthy Subjects

Cheu et al AJRCC 2006
Central Sleep Apnea in Heart Failure-Cheyne Stokes respiration
Induced Periodic Breathing and CBFV in CHF

Patient with HF and no CSA

Patient with HF and CSA

Xie et al 2005
Changes in AH1 and CAI before and 6 months after induction of carvedilol in five patients with CAI > 5 at baseline
Relation between PCWP and AHI in Patients with HF and CSA: Effect of Optimal CHF Management on CSA

Naughton et al 1999
Treatment of CSA with Adaptive Servo Ventilation - Teschler et al AJRCC2001
SBD and Heart Failure in Clinical Practice

Congestive heart failure

Diastolic dysfunction

Coronary disease or hypertension

Systolic dysfunction

OSA

CSA

OSA
If SDB is highly prevalent in patients with heart failure, and it worsens outcomes, why are we not routinely screening for it?

- Criteria for case finding:
  - Highly prevalent disorder
  - Known negative impact
  - Treatable disorder
  - Feasibility of identification

» WHO 1966- Jungner
Pathway - Enter Orders

Name: [REDACTED]  MR#: 907362285  Svc: CHF

<table>
<thead>
<tr>
<th>Line #</th>
<th>Dept</th>
<th>Description</th>
<th>Rqst D/Tm</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>p---</td>
<td>ADM HR Failure MGMT</td>
<td>11/07 1534</td>
</tr>
<tr>
<td>2</td>
<td>NUR</td>
<td>VITAL SIGNS: Q4HVS</td>
<td>11/07 1600</td>
</tr>
<tr>
<td>3</td>
<td>NUR</td>
<td>ACTIVITY BEDREST W/ BP R **</td>
<td>11/07 1534</td>
</tr>
<tr>
<td>4</td>
<td>NUR</td>
<td>ECG STAT UD/PRN: CONT</td>
<td>11/07 1534</td>
</tr>
<tr>
<td>5</td>
<td>NUR</td>
<td>IV MANAGEMENT:</td>
<td>11/07 1534</td>
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<tr>
<td>6</td>
<td>NUR</td>
<td>CARDIAC MONITORING CONT</td>
<td>11/07 1534</td>
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<tr>
<td>7</td>
<td>NUR</td>
<td>WEIGHT QDAYS</td>
<td>11/08 0900</td>
</tr>
<tr>
<td>8</td>
<td>PUL</td>
<td>PORTABLE SLEEP STUDY - ROSS UNIT ONCE</td>
<td>11/07 1534</td>
</tr>
<tr>
<td>9</td>
<td>R/T</td>
<td>PULSE QXIOMETRY ONCE</td>
<td>11/07 1534</td>
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<tr>
<td>10</td>
<td>DTY</td>
<td>CARDIAC-4GM NA</td>
<td>11/08 0630</td>
</tr>
<tr>
<td>11</td>
<td>PHM</td>
<td>DOUCASTE ORAL 100 MG ORAL BIDPRN</td>
<td>11/07 1534</td>
</tr>
<tr>
<td>12</td>
<td>PHM</td>
<td>DIPHENHYDRAMINE 25 MG ORAL QHSPRN</td>
<td>11/07 1534</td>
</tr>
<tr>
<td>13</td>
<td>PHM</td>
<td>SODIUM CHLORIDE 2.5ML FLUSH 2.5 ML IVP Q8H</td>
<td>11/07 2200</td>
</tr>
<tr>
<td>14</td>
<td>PHM</td>
<td>ACETAMINOPHEN 650 MG ORAL Q6HPRN</td>
<td>11/07 1534</td>
</tr>
</tbody>
</table>

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[F2 Census]  [F5 Show ingrd]  [F6 Rvw/Revise]  [F11 MORE PUL]  [F12 Sign]

[F5 LAST]
63 y/o OSA with long circulatory time
ADHF patients hospitalized between 12/30/06 and 1/31/08 (n=559)

ADHF and no known SDB (n=466)

Unsuccessful recording (n=71)

No SDB (n=97) 25%

ADHF patients with successful recording (n=395)

SDB (n=298) 75%

OSA (n=226) 57%

OSA validation cohort (n=111)

Patients returned (n=62) 56%, all classified as OSA

CSA (n=72) 18%

CSA validation cohort (n=26)

Patients returned (n=12) reclassified as OSA

Excluded patients with ADHF and self reported existing SDB (n=93)

Khayat et al JCF-2009
Prevalence of OSA in ADHF Patients

- Patients admitted to the Ross hospital with ADHF
- Inpatients sleep studies on day 1-2 on all new admission
- No selection on part of treating physicians or nurses
- Automatic COE, Network and staff initiated studies
## Characteristics of Patients with ADHF

<table>
<thead>
<tr>
<th>Patient characteristic</th>
<th>Mean or % (SE)</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>59 (0.7)</td>
<td>(57, 60)</td>
</tr>
<tr>
<td><strong>Sex (male)</strong></td>
<td>62 % (2%)</td>
<td>(58 %, 67 %)</td>
</tr>
<tr>
<td><strong>Ischemic cardiomyopathy</strong></td>
<td>57 (0.8)</td>
<td>(56, 59)</td>
</tr>
<tr>
<td><strong>Left ventricular ejection fraction</strong></td>
<td>33 (0.9)</td>
<td>(32, 35)</td>
</tr>
<tr>
<td><strong>BMI kg/cm2</strong></td>
<td>32 (0.4)</td>
<td>(31, 33)</td>
</tr>
<tr>
<td><strong>Admission BNP pg/mL</strong></td>
<td>888 (59)</td>
<td>(773, 1003)</td>
</tr>
<tr>
<td><strong>Atrial fibrillation</strong></td>
<td>35 % (2%)</td>
<td>(30 %, 39 %)</td>
</tr>
</tbody>
</table>

Khayat et al JCF-2009
<table>
<thead>
<tr>
<th></th>
<th>OSA Mean (SE)</th>
<th>CSA Mean (SE)</th>
<th>Negative Mean (SE)</th>
<th>Negative vs. OSA P value</th>
<th>Negative vs. CSA P value</th>
<th>CSA vs. OSA P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>60 (0.9)</td>
<td>58 (1.8)</td>
<td>56 (1.6)</td>
<td>0.03</td>
<td>0.37</td>
<td>0.40</td>
</tr>
<tr>
<td>Male</td>
<td>69% (3%)</td>
<td>75% (5%)</td>
<td>38% (5%)</td>
<td>0.0001</td>
<td>0.0001</td>
<td>0.30</td>
</tr>
<tr>
<td>Ischemic</td>
<td>62% (3%)</td>
<td>64% (6%)</td>
<td>44% (5%)</td>
<td>0.003</td>
<td>0.01</td>
<td>0.82</td>
</tr>
<tr>
<td>Dilated</td>
<td>23% (3%)</td>
<td>14% (4%)</td>
<td>35% (5%)</td>
<td>0.02</td>
<td>0.001</td>
<td>0.11</td>
</tr>
<tr>
<td>Others</td>
<td>15% (2%)</td>
<td>22% (5%)</td>
<td>21% (4%)</td>
<td>0.22</td>
<td>0.80</td>
<td>0.16</td>
</tr>
<tr>
<td>LVEF</td>
<td>34 (1.2)</td>
<td>27 (1.7)</td>
<td>38 (1.8)</td>
<td>0.06</td>
<td>0.0001</td>
<td>0.0008</td>
</tr>
<tr>
<td>BMI</td>
<td>33 (0.6)</td>
<td>29 (0.9)</td>
<td>31 (0.8)</td>
<td>0.03</td>
<td>0.12</td>
<td>0.0001</td>
</tr>
<tr>
<td>LVEDD</td>
<td>57 (1.1)</td>
<td>63 (1.6)</td>
<td>54 (1.2)</td>
<td>0.14</td>
<td>0.0001</td>
<td>0.0037</td>
</tr>
<tr>
<td>BNP</td>
<td>746 (66)</td>
<td>1341 (161)</td>
<td>873 (130)</td>
<td>0.35</td>
<td>0.02</td>
<td>0.001</td>
</tr>
<tr>
<td>A-fib</td>
<td>39% (3%)</td>
<td>32% (6%)</td>
<td>28% (5%)</td>
<td>0.06</td>
<td>0.57</td>
<td>0.31</td>
</tr>
</tbody>
</table>

Khayat et al. JCF-2009
### Predictors of SDB in all patients with ADHF

<table>
<thead>
<tr>
<th>Variable Names</th>
<th>Pearson Correlation Coefficients</th>
<th>Number of Patients</th>
<th>95% Confidence Limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>AHI with EF</td>
<td>-0.10</td>
<td>370</td>
<td>(-0.20, 0.00)</td>
</tr>
<tr>
<td>AHI with LVEDD</td>
<td>0.19</td>
<td>281</td>
<td>(0.07, 0.30)</td>
</tr>
<tr>
<td>AHI with BMI</td>
<td>0.17</td>
<td>393</td>
<td>(0.07, 0.26)</td>
</tr>
<tr>
<td>AHI with A-Fib</td>
<td>-0.02</td>
<td>394</td>
<td>(-0.12, 0.08)</td>
</tr>
<tr>
<td>AHI with Age</td>
<td>0.02</td>
<td>395</td>
<td>(-0.08, 0.12)</td>
</tr>
<tr>
<td>AHI with BNP</td>
<td>0.004</td>
<td>294</td>
<td>(-0.11, 0.12)</td>
</tr>
</tbody>
</table>

### Predictors of AHI in all patients with ADHF and SDB

<table>
<thead>
<tr>
<th>Variable Names</th>
<th>Pearson Correlation Coefficients</th>
<th>Number of Patients</th>
<th>95% Confidence Limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>AHI with EF</td>
<td>-0.01</td>
<td>279</td>
<td>(-0.13, 0.11)</td>
</tr>
<tr>
<td>AHI with LVEDD</td>
<td>0.15</td>
<td>212</td>
<td>(0.01, 0.28)</td>
</tr>
<tr>
<td>AHI with BMI</td>
<td>0.18</td>
<td>298</td>
<td>(0.07, 0.29)</td>
</tr>
<tr>
<td>AHI with Age</td>
<td>-0.06</td>
<td>298</td>
<td>(-0.17, 0.05)</td>
</tr>
<tr>
<td>AHI with BNP</td>
<td>-0.006</td>
<td>231</td>
<td>(-0.13, 0.12)</td>
</tr>
</tbody>
</table>
‡ indicates a significant difference negative vs. OSDB (p value < 0.05),
† indicates a significant difference negative vs. CSDB (p value < 0.05),
* indicates a significant difference CSDB vs. OSDB (p value < 0.05)
### Comparison of AHI between the in-hospital study and the polysomnography in the validated OSA and CSA patients

<table>
<thead>
<tr>
<th></th>
<th>PSG AHI Mean (SE) (N)</th>
<th>Inpatient AHI Mean (SE) (N)</th>
<th>Difference between PSG AHI and Inpatient AHI</th>
<th>95% CI for the Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>OSA</strong></td>
<td>41.7 (3.9) (62)</td>
<td>37.4 (2.5) (62)</td>
<td>4.3</td>
<td>-1.1, 9.6</td>
</tr>
<tr>
<td><strong>CSA</strong></td>
<td>36.4 (7.2) (12)</td>
<td>49.1 (5.9) (12)</td>
<td>-12.7</td>
<td>-29.9, 4.5</td>
</tr>
</tbody>
</table>

Khayat et al JCF-2009
Prevalence of SDB in Patients with ADHF

- SDB is present in 75% of patients
- OSA is more prevalent than CSA (57% vs. 18%)
- Increased LVEDD predicted having CSA
- Increased BMI predicted having OSA
- No other predictors of SDB and high prevalence support need for routine screening.
Role of OSA in the Acute Decompensation of heart Failure


- Contractile function
- Sympathetic activity
- Hemodynamic measurements
- Oxygenation
- Functional Status
patients with ADHF criteria hospitalized 12/2006-4/2008 (n=401)

Successful in-hospital sleep study (n=232)

No SDB (n=44)
Obstructive SDB (n=145)
Central SDB (n=43)

Met Inclusion Criteria and Consented* (n=46)

Control Arm (standard treatment of ADHF)
1 death, 2 LVAD, 1 dropped out
19 patients reached conclusion

Intervention Arm (standard ADHF treatment + APAP)
1 death, 1 LVAD
21 patients reached conclusion

Khayat et al Chest 2009
### Effect of In Hospital APAP on Cardiac Function three days post-randomization

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Treatment</th>
<th>Difference (APAP Effects) (p-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LVEF</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>three days post randomization</td>
<td>25.8</td>
<td>30.4</td>
<td>4.6 (0.031)</td>
</tr>
<tr>
<td>change from base line (Final – Baseline)</td>
<td>-0.2</td>
<td>4.4</td>
<td></td>
</tr>
<tr>
<td><strong>LVESV</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>three days post randomization</td>
<td>169</td>
<td>144</td>
<td>-24.8 (0.0007)</td>
</tr>
<tr>
<td>change from base line (Final – Baseline)</td>
<td>3.2</td>
<td>-22.1</td>
<td></td>
</tr>
<tr>
<td><strong>LVEDV</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>three days post randomization</td>
<td>228</td>
<td>204</td>
<td>-23.9 (0.03)</td>
</tr>
<tr>
<td>change from base line (Final – Baseline)</td>
<td>2.1</td>
<td>-22</td>
<td></td>
</tr>
</tbody>
</table>
Effect of In-hospital APAP on 3-Days LVEF

Khayat et al. Chest 2009
## Sensitivity Analysis of APAP Effect on LVEF in Patients with ADHF

<table>
<thead>
<tr>
<th>Covariate Adjustments</th>
<th>APAP Effect</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AHI</td>
<td>5.1</td>
<td>0.02</td>
</tr>
<tr>
<td>BMI</td>
<td>4.5</td>
<td>0.04</td>
</tr>
<tr>
<td>Cardiomyopathy Type</td>
<td>4.5</td>
<td>0.04</td>
</tr>
<tr>
<td>Gender</td>
<td>4.3</td>
<td>0.04</td>
</tr>
</tbody>
</table>

### Interaction Effects with Median Split of Baseline Variable

<table>
<thead>
<tr>
<th></th>
<th>APAP Effect for &lt; Median</th>
<th>APAP Effect for &gt; Median</th>
<th>Interaction Effect (difference between effects)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>p-value</td>
</tr>
<tr>
<td>LVEF</td>
<td>3.9</td>
<td>4.9</td>
<td>0.8</td>
</tr>
<tr>
<td>AHI</td>
<td>9.2</td>
<td>2</td>
<td>0.08</td>
</tr>
<tr>
<td>BMI</td>
<td>4.7</td>
<td>3.6</td>
<td>0.8</td>
</tr>
<tr>
<td>BNP</td>
<td>4.9</td>
<td>5.3</td>
<td>0.9</td>
</tr>
<tr>
<td>Cardiomyopathy Type</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic</td>
<td>4.1</td>
<td>6.4</td>
<td>0.7</td>
</tr>
</tbody>
</table>

Khayat et al Chest 2009
# Effect of PAP on hemodynamic and neurohumoral measures

<table>
<thead>
<tr>
<th>Change from baseline</th>
<th>Control</th>
<th>Treatment</th>
<th>Difference (p-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary Norepinephrine</td>
<td>-0.003</td>
<td>-0.011</td>
<td>-0.0008 (0.18)</td>
</tr>
<tr>
<td>BNP</td>
<td>17</td>
<td>-457</td>
<td>-474 (0.13)</td>
</tr>
<tr>
<td>BUN</td>
<td>-2.4</td>
<td>1.6</td>
<td>4.1 (0.18)</td>
</tr>
<tr>
<td>Creatinine</td>
<td>-0.03</td>
<td>0.21</td>
<td>-0.24 (0.19)</td>
</tr>
<tr>
<td>Systolic BP</td>
<td>-5.2</td>
<td>-6.5</td>
<td>-1.3 (0.78)</td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>-1.2</td>
<td>-3</td>
<td>-1.9 (0.6)</td>
</tr>
<tr>
<td>Weight</td>
<td>-0.5</td>
<td>-2</td>
<td>-1.5 (0.048)</td>
</tr>
</tbody>
</table>

Khayat et al Chest 2009
Inpatient Treatment of OSA during ADHF

• Safe
• Improved LVEF; effect on long term cardiac outcomes and adherence is currently under evaluation.
• Feasible in a high risk population
• Requires expertise and training
• Associated with “excellent” tolerance and adherence