CPAP: Treatment of Choice for OSA

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Disclosure:
Nothing to disclose

CPAP

- Among CPAP adherent patients, outcomes are excellent.
- Alleviates UA obstruction in essentially everyone.
- Many patients are either lost to follow-up or never come to clinical fruition to avoid “the mask”.
- Such patients never enter randomized clinical trials of CPAP therapy.
- True adherence in clinical practice is hard to estimate e.g. many patients refuse to see me.

Why is CPAP the treatment of choice for obstructive sleep apnea?
**Effect of CPAP on ESS**

- Change in ESS
  -2 0 2 4 6

Combined

- Engleman 1998
- Henke 2001
- Montserrat 2001
- Barbe 2001
- Ballester 1999
- Redline 1998
- Engleman 1999
- Monasterio 2001
- Faccenda 2001

Mean improvement in ESS of 2.94

*Arch Intern Med. 2003 163:565-71*

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**CPAP Appears to Be Cost Effective**

- Middle aged men and women (30-60yrs) with newly diagnosed sleep apnea
- 70% compliance with CPAP (3 months of therapy)
- Direct medical costs over five years:
  - CPAP: $4103, 2.41 QALY
  - No CPAP: $2071, 1.49 QALY
  - $2032/QALY saved
- Direct and indirect costs:
  - CPAP was cost-savings to society
  - CPAP was less costly than no CPAP ($7773 vs $11,121) while resulting in a gain in QALY

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**Association Between Treated and Untreated Obstructive Sleep Apnea and Risk of Hypertension**

- Joel M. Marin, MD

**Context:** Systemic hypertension is prevalent among patients with obstructive sleep apnea.

**Table 4:** Cox Proportional Hazards Regression Models of Incident Hypertension in Patients With OSA With Multiple Imputations

<table>
<thead>
<tr>
<th></th>
<th>Indicative for CPAP Therapy</th>
<th>Declined CPAP Therapy</th>
<th>Not Indicated for CPAP Therapy</th>
<th>Treated With CPAP Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(Hazard Ratio (95% CI))</td>
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</tr>
<tr>
<td>Model 1, adjusted for age, sex, and BMI</td>
<td>1.22 (1.13, 1.32)</td>
<td>2.05 (1.89, 2.22)</td>
<td>2.70 (1.90, 3.85)</td>
<td>1.47 (1.24, 1.70)</td>
</tr>
<tr>
<td>Model 2, adjusted for BMI and OSA</td>
<td>1.27 (1.20, 2.06)</td>
<td>2.76 (2.06, 3.79)</td>
<td>2.60 (1.76, 3.66)</td>
<td>1.17 (0.90, 1.56)</td>
</tr>
<tr>
<td>Model 3, adjusted for BMI, OSA, and change in BMI</td>
<td>1.24 (1.18, 1.31)</td>
<td>2.14 (1.86, 2.49)</td>
<td>2.05 (1.56, 2.71)</td>
<td>1.60 (1.32, 1.93)</td>
</tr>
<tr>
<td>Model 4, adjusted for baseline variables</td>
<td>1.24 (1.15, 1.34)</td>
<td>2.23 (1.94, 2.55)</td>
<td>2.05 (1.60, 2.66)</td>
<td>2.05 (1.60, 2.66)</td>
</tr>
</tbody>
</table>

Marin et al. JAMA 2012

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**Figure 2:** Forest plots comparing the effects of PAP and control on (A) diurnal SBP, and (B) diurnal DBP

- PAP appears to be effective in reducing blood pressure.
Continuous Positive Airway Pressure Treatment Improves Pulmonary Hemodynamics in Patients with Obstructive Sleep Apnea

- Link has been debated
- Need ABG abnormality during daytime
- Mild to moderate PH seen with OSA alone
- Marked hypoxic vasoreactivity
- Reversible with CPAP

Pepin et al. AJRCCM 2010

CPAP effect on BP

- Effect appears modest
- Studies do not assess nocturnal acute fluctuations which can be large
- Partially dependent on adherence with CPAP therapy
- Medications are much better than CPAP (Valsartan vs. CPAP)
- Room for improvement

Sajkov et al AJRCCM 2002
How Good Are the CPAP Data?

- Discuss some frequently cited data
- Some of the current studies are flawed

Recurrence of AFIB after Cardioversion in Untreated OSA

- *p<0.009 compared to controls
- **p<0.013 compared to treated OSA

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Not an RCT – based on CPAP adherence
Conclusion: Patients consistently refilling lipid-lowering medications were more adherent to CPAP, suggesting that differences in medication adherence or other health-promoting behaviors should be investigated in future nonrandomized, observational studies linking CPAP adherence and cardiovascular outcomes.

Table 3— Adjusted Odds Ratios for Adequate Initial Adherence to CPAP (N = 117)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Adjusted OR (95% CI) P Value</th>
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<tbody>
<tr>
<td>Lipid medication adherence (≥50%)</td>
<td>1.8 (1.0-3.3) .04</td>
</tr>
<tr>
<td>Age (per 10y increase)</td>
<td>1.6 (1.0-2.5) .04</td>
</tr>
<tr>
<td>Race: Black (yes/white/other?)</td>
<td>0.9 (0.5-1.5) .55</td>
</tr>
<tr>
<td>BMI (per SD change)</td>
<td>0.9 (0.6-1.5) .10</td>
</tr>
<tr>
<td>Echocardiographic index (per SD change)</td>
<td>1.1 (1.0-3.5) .41</td>
</tr>
<tr>
<td>Apnea-hypopnea index (per SD change)</td>
<td>1.0 (0.8-1.3) .91</td>
</tr>
<tr>
<td>Diagnostic sleep study, unattended</td>
<td>1.2 (0.7-2.2) .44</td>
</tr>
<tr>
<td>First night of CPAP use (yes/no subsequent nights)</td>
<td>0.4 (0.2-0.6) &lt;.001</td>
</tr>
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</table>

Findings: 264 healthy men, 377 simple snorers, 440 with untreated mild-moderate obstructive sleep apnea-hypopnea, 225 with untreated severe disease, and 322 with the disease and treated with CPAP were included in the analysis. Patients with untreated severe disease had a higher incidence of fatal cardiovascular events (1.06 per 100 person-years) and nonfatal cardiovascular events (2.33 per 100 person-years) than did patients with mild-moderate disease (0.35, p = .02 and 0.59, p = .0004). Simple snorers (0.14, p = .0006 and 0.18, p = .0001), patients treated with CPAP (0.35, p = .0008 and 0.64, p = .0004), and healthy participants (0.3, p = .001 and 0.45, p = .0004). Multivariate analysis, adjusted for potential confounders, showed that untreated severe obstructive sleep apnea-hypopnea significantly increased the risk of fatal (odds ratio 2.87, 95% CI 1.27-7.51) and nonfatal (1.17, 1.12-7.51) cardiovascular events as compared with healthy participants.

Interpretation: In men, severe obstructive sleep apnea-hypopnea significantly increases the risk of fatal and non-fatal cardiovascular events. CPAP treatment reduces this risk.

Marin caveats

- Not a randomized trial
- Adherent patients always do better in trials
- May be a marker of good prognosis rather than a CPAP effect per se
- Hard to believe CPAP would bring risk to that of healthy controls despite more diabetes, HTN etc

Long-term cardiovascular outcomes in men with obstructive sleep apnea-hypopnea with or without treatment with continuous positive airway pressure: an observational study

(A.M. Marin, Santiago Carughi, Koganesi Vuente, A. Ch Ayestat)

Summary

Background: The effect of obstructive sleep apnea-hypopnea as a cardiovascular risk factor and the potential protective effect of its treatment with continuous positive airway pressure (CPAP) is unclear. We did an observational study to compare incidence of fatal and non-fatal cardiovascular events in simple snorers, patients with untreated obstructive sleep apnea-hypopnea, patients treated with CPAP, and healthy men recruited from the general population.

Methods: We recruited men with obstructive sleep apnea-hypopnea or simple snorers from a sleep clinic and a population-based sample of healthy men, matched for age and body mass index with the patients with untreated severe obstructive sleep apnea-hypopnea. The presence and severity of the disorder was determined with full polysomnography and the apnea-hypopnea index (AHI) was calculated as the average number of apneas and hypopneas per hour of sleep. Participants were followed up at least once per year for a mean of 10.1 ± 3 years (SD 1.4) and CPAP compliance was checked with the breath meter. Endpoints were fatal cardiovascular events (death from myocardial infarction or stroke) and nonfatal cardiovascular events (nonfatal myocardial infarction, nonfatal stroke, coronary artery bypass surgery, and percutaneous transluminal coronary angiography).

Findings: 264 healthy men, 377 simple snorers, 440 with untreated mild-moderate obstructive sleep apnea-hypopnea, 225 with untreated severe disease, and 322 with the disease and treated with CPAP were included in the analysis. Patients with untreated severe disease had a higher incidence of fatal cardiovascular events (1.06 per 100 person-years) and nonfatal cardiovascular events (2.33 per 100 person-years) than did patients with mild-moderate disease (0.35, p = .02 and 0.59, p = .0004). Simple snorers (0.14, p = .0006 and 0.18, p = .0001), patients treated with CPAP (0.35, p = .0008 and 0.64, p = .0004), and healthy participants (0.3, p = .001 and 0.45, p = .0004). Multivariate analysis, adjusted for potential confounders, showed that untreated severe obstructive sleep apnea-hypopnea significantly increased the risk of fatal (odds ratio 2.87, 95% CI 1.27-7.51) and nonfatal (1.17, 1.12-7.51) cardiovascular events as compared with healthy participants.

Interpretation: In men, severe obstructive sleep apnea-hypopnea significantly increases the risk of fatal and non-fatal cardiovascular events. CPAP treatment reduces this risk.
Studies looking at Pre vs. Post CPAP are often flawed since the diagnosis is not occurring at random (ascertainment bias).

Relative Risk of MVC Post CPAP compared to pre-CPAP

Pooled estimate: 0.204 (0.18-0.22)  Archives 2006
Weaver et al 2004

CPAP vs. UPPP

- Not a randomized trial
- UPPP patients do not have to be adherent
- Among 100 CPAP treated patients, only a percentage will get the maximal benefit due to adherence issues
- Among 100 UPPP patients, all will experience some effects, even if modest overall.

Analogy

- Anti-arrhythmic drugs don’t really work
- AICDs do work
- Taking patient adherence off the table can be beneficial.
CPAP Conclusions

- CPAP is the treatment of choice for OSA
- Much of the data is from clinical trials that enroll highly motivated patients
- “Treatment adherent” analyses are flawed
- Not clear how much it helps cardiovascular consequences
- Removing patient adherence from the equation is likely to improve outcomes
- Substantial room for improvement in OSA therapy – i.e. improved adherence, new therapies

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