Pro: CPAP Improves CV Outcomes in OSA

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JAMA | Original Investigation
Association of Positive Airway Pressure With Cardiovascular Events and Death in Adults With Sleep Apnea
A Systematic Review and Meta-analysis

CONCLUSIONS AND RELEVANCE The use of PAP, compared with no treatment or sham, was not associated with reduced risks of cardiovascular outcomes or death for patients with sleep apnea. Although there are other benefits of treatment with PAP for sleep apnea, these findings do not support treatment with PAP with a goal of prevention of these outcomes.

Yu et al. JAMA 2017;318(2):156-166
Effect of CPAP on incidence of HTN and CV events in nonsleepy patients with OSA

Mean CPAP use ranged from 0 to 8.76 hr/day
Median use = 5.0 hr/day (IQR, 2.18-6.35)

Barbé et al. *JAMA* 2012; 307:2161-2168

Cumulative incidence of hypertension or cardiovascular events during follow-up

Barbé et al. *JAMA* 2012; 307:2161-2168
ASV for central sleep apnea in systolic heart failure – Serve-HF trial

Cowie MR et al. NEJM 2015;373:1095-1105

Average ASV device usage over time
Serve-HF trial

Cowie MR et al. NEJM 2015;373:1095-1105
CPAP for prevention of cardiovascular events in OSA (SAVE)

- In a pre-specified analysis of propensity-score matched patients, those using CPAP > 4 hr/day had a statistically significantly lower risk of a cerebrovascular event compared to those with adherence < 4 hr/day
- Although propensity matching has become popular in observational studies to control for confounding by indication, its ability to control for confounding by a post-randomization factor such as adherence is uncertain.
Assess lifestyle behavior
to control for healthy user bias

In addition to the usual covariates (age, gender, race, prescribed meds, alcohol consumption, smoking) should we also be measuring:

**Lifestyle factor**
- Medication adherence
- Clinic attendance
- Physical activity
- Diet

**Measurement**
- Medication possession rate
- Clinic appointment show rate
- Waist accelerometry
- Questionnaire?

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**Obstructive Sleep Apnea**

- Chronic intermittent hypoxia
- Arousal related stimuli
- ↑ NADPH oxidase
- Circulating inflammatory biomarkers

**Oxidative Stress**

- Urinary isoprostanes
- Urinary catecholamines

**Sympathetic activity**

- Renin
- Aldosterone
- RAAS
- Endothelin-1*

**Inflammatory activity**

- Endothelial dysfunction
- Flow-mediated dilatation

*Sympathetic activation due to activation of carotid body and central neurons controlling sympathetic output. Blue boxes indicate assessment measures.
Effect of CPAP treatment on mean ambulatory blood pressure

Mean net change in systolic BP

Study Name

Differences in means and 95% CI

Overall SBP decrease -2.6 mm Hg

Increased SBP

Decreased SBP

Effects of CPAP on BP in patients with resistant HTN and OSA: A meta-analysis

<table>
<thead>
<tr>
<th>Study Name</th>
<th>Statistics for each study</th>
<th>Differences in means and 95% CI</th>
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<tbody>
<tr>
<td></td>
<td>Difference in means</td>
<td>Lower limit</td>
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<td>Logan 2003</td>
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<td>Garcia 2007</td>
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Overall SBP decrease -7.2 mm Hg


Does CPAP Improve CV Outcomes in OSA? The Jury is Still Out!

- The RCTs reporting no improvement in CV outcomes following PAP treatment are flawed:
  - Inadequate PAP adherence
  - Inadequately powered
  - Exclusion of patient with severe OSA
- Strong evidence that CPAP treatment reduces blood pressure in hypertensive OSA patients
- Strong evidence that CPAP treatment improves sympathetic activity and other known intermediary factors associated with CV disease