Sleep Apnea in Older Adults

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Disclosures

Current Funding: none

Leadership position
- American College of Chest Physicians, President-elect
- National Board of Respiratory Care

Expert Witness
- Kinnard, Clayton, Beveridge LLC (perioperative death from OSA)
- Kinkead Stiltz, PLLC (noisy bar below condominium)

Honorarium
- CHEST Review, CCM International

Conflicts of Interest: I personally am not getting any younger.
Overview

Significance

State-of-the-art knowledge

Knowledge gaps

Research opportunities
Figure 1. Smoothed plot (5-year moving average) of the prevalence of an apnea-hypopnea index (AHI) of 15 or greater by age.
The effects of gender and BMI change with aging.

AFTER THE AGE OF 50, GENDER BECOMES LESS IMPORTANT

AFTER THE AGE OF 60, BMI BECOMES LESS IMPORTANT

Weight is a more important risk factor for men than for women

Age is a more important risk factor for women than for men.

(Tishler P, 2003)
Potential Factors for Increased OSA Risk in Older People

- Increased body weight
- Reduced pulmonary function
- Impaired ventilatory control
- Increased upper airway collapsibility
- Reduced muscular endurance
- Impaired thyroid function
- Increased sleep fragmentation
- Reduced slow wave sleep
Changes in airway anatomy with age - MRI findings

- Soft palate gets longer
- Pharyngeal fat pads increase in size
- Shape of bony structures around pharyngeal airway change
- Response of genioglossus muscle to negative pressure stimulation diminishes

Consequences of Sleep Apnea: Most Data is from Middle-Aged People

- Sleepiness
- Impaired quality of life
- Decreased cognitive function
- Increased hospitalizations and health care costs
- Increased car accidents
- Impaired glucose control
- Hypertension
- Increased cardiac risk
- Increased mortality rate
- Impotence
What About Studies or Conditions of Older People?

- Stroke
- Atrial fibrillation
- Nocturia
- Hypertension
- Cardiovascular disease
- Death
Stroke or Death with OSA
Yaggi HK, N Engl J Med 2005, n=1022, mean age ~ 60

Figure 1. Kaplan–Meier Estimates of the Probability of Event-free Survival among Patients with the Obstructive Sleep Apnea Syndrome and Controls.
Recurrence of Atrial Fibrillation Following Cardioversion in Patients with OSA (Kanagala Circ 2003, Mean age 66 years)

* $p < 0.009$ compared to controls
** $p < 0.013$ compared to treated OSA
CPAP Associated with Less Likelihood of Chronic AF
(Holmqvist F, Am Heart J 2015, n=10,132)

Mean age
OSA  69
No OSA  76
Nocturia Correlates (Weakly) with RDI (Margel D, Urology 2006)

**FIGURE 1.** Correlation between number of awakenings to void before treatment with respiratory disturbance index ($r = 0.25, P = 0.01$).
CPAP Improves Nocturia
(Margel D, Urology, 2006; n=50, mean age 55)

FIGURE 2. Comparison of outcomes of 50 patients with mild to moderate OSA (RDI less than 35/hour) and 47 with severe OSA (RDI greater than 35/hour).
From The Joint National Committee on Hypertension 7

**DIAGNOSTIC WORKUP OF HYPERTENSION**
- Assess risk factors and comorbidities.
- Reveal identifiable causes of hypertension.
- Assess presence of target organ damage.
- Conduct history and physical examination.
- Obtain laboratory tests: urinalysis, blood glucose, hematocrit and lipid panel, serum potassium, creatinine, and calcium. Optional: urinary albumin/creatinine ratio.
- Obtain electrocardiogram.

**ASSESS FOR MAJOR CARDIOVASCULAR DISEASE (CVD) RISK FACTORS**
- Hypertension
- Obesity (body mass index ≥30 kg/m²)
- Dyslipidemia
- Diabetes mellitus
- Cigarette smoking
- Physical inactivity
- Microalbuminuria, estimated glomerular filtration rate <60 ml/min
- Age (>55 for men, >65 for women)
- Family history of premature CVD (men age <55, women age <65)

**ASSESS FOR IDENTIFIABLE CAUSES OF HYPERTENSION**
- Sleep apnea
- Drug-induced related
- Chronic kidney disease
- Primary aldosteronism
- Renovascular disease
- Cushing's syndrome or steroid therapy
- Pheochromocytoma
- Coarctation of aorta
- Thyroid/parathyroid disease

**ALGORITHM FOR TREATMENT OF HYPERTENSION**

**LIFESTYLE MODIFICATIONS**

**INITIAL DRUG CHOICES**
- Without Compelling Indications
- With Compelling Indications

**Stage 1 Hypertension** (SBP 140-159 or DBP 90-99 mmHg)
- Thiazide-type diuretics for most. May consider ACEI, ARB, BB, CCB, or combination.

**Stage 2 Hypertension** (SBP ≥160 or DBP ≥100 mmHg)
- 2-drug combination for most (usually thiazide-type diuretic and ACEI, or ARB, or BB, or CCB).

**Optimize dosages or add additional drugs until goal blood pressure is achieved. Consider consultation with hypertension specialist.**

See Strategies for Improving Adherence to Therapy.
Meta-analysis of CPAP and Systolic Blood Pressure (Fava C Chest 2014)

<table>
<thead>
<tr>
<th>Study name</th>
<th>Difference in means</th>
<th>Lower limit</th>
<th>Upper limit</th>
<th>p-Value</th>
<th>Relative weight</th>
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<td>Arias MA et al. 2005</td>
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<td>Ruttaanumpawan P et al. 2008</td>
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<td>8,100</td>
<td>1,775</td>
<td>14,425</td>
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<td><strong>Overall effect</strong></td>
<td>2,559</td>
<td>1,437</td>
<td>3,681</td>
<td>0,000</td>
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Incident Hypertension in Non-sleepy Patients
(Barbe F, JAMA 2012, n=723) Mean age ~ 51
Death in Seniors with OSA (Martinez Garcia MA, AJRCCM 2012) Mean age 71

- All-cause (n=190)
- Malignancy (n=38)
- Cardiovascular (n=100)
- Stroke (n=28)
- Heart failure (n=37)
- Myocardial infarction (n=31)

HR (95% CI)
CPAP Treatment and 6-Year Mortality in the Elderly (~ 71 yrs) (Martinez Garcia MA, AJRCCM 2012)

![Graph showing cumulative mortality over follow-up years for different categories of treatment: Severe untreated, Mild to moderate, Treated, Control.](image-url)
Sleep Apnea, CPAP and Death (OSA not defined)
Jennum P, Nat Sci Sleep 2015, n=25,389

[Survival curve diagram]
Overview

Significance

State-of-the-art knowledge

Knowledge gaps

Research opportunities
Cognitive Function and OSA
Rosenzweig I Lancet Respir Med 2015

Cognitive deficits most strongly associated with OSA:

- Attention/vigilance
- Visuospatial and constructional abilities
- Executive function
- Delayed visual and verbal memory

Cognitive dysfunction correlate with severity of hypoxemia; but attention/vigilance correlates with sleep fragmentation (Buck R Respirology 2013).

Patients with severe OSA had impressive recovery of white matter and improvement in memory, attention and executive functioning at 2 years (Castronovo V Sleep 201).

Patients with OSA had improved cognition and increased grey matter after 3 months of CPAP (Kohler, Expert Opin Investig Drugs 2009).

Patients with severe OSA and AD who used CPAP had slower decline over 3 years than those untreated (Troussiere AC J Neurol Neurosurg Psychiatry 2014).

Questions remain about duration/timing of treatment, which deficits are causal and reversible.
Patients with OSA were significantly younger at MCI and AD-dementia onset.

CPAP treatment reduced this effect.

(N=767 “OSA” self-reported)

Osoria R, Neurology 2015
Intermittent Hypoxia (IH) • Short, mild, lower cycle frequency IH is believed to generate adaptive responses in the brain, ie ischemic preconditioning.

• Chronic severe high frequency IH results in disruption of homeostatic mechanisms and inflammation.
Pharyngeal obstruction

Intermittent hypoxia, Sleep fragmentation

Brain injury

Hypotrophic changes

- Medial prefrontal cortex and anterior cingulate cortex
- Thalamus
- Parahippocampal gyrus
- Inferior temporal gyrus
- Hippocampus
- Posterior lateral parietal cortex
- Cerebellum

CPAP, Ischaemic (pre)conditioning

Amelioration

↓ Grey matter, ↓ myelination of white matter tracts, EEG changes and slowing, ↓ cerebral perfusion, impairment in respective cognitive and emotional domains
RCT of CPAP and cognitive function in OSA.

“OSA” defined as AHI > 10, but apnea and hypopnea not defined in primary article.

1098 participants, about 2/3s male, mean age about 52, mean BMI about 32. Severely hypoxemic patients were excluded.

NO difference in primary outcomes at 6 months, tho CPAP treated patients were less sleepy.

Editorial argues that this suggests that cognitive impairment is irreversible, but preventable. (Schwartz SW Sleep 2012)
• OSA is associated with cardiovascular risk factors and comorbidities, BUT
• Mild to moderate intermittent hypoxemia appears to result in ischemic preconditioning in both animals and humans.
• Ischemic preconditioning likely the cells' ability to maintain homeostatic redox balance by upregulation of cytoprotective genes responsible for promoting the cells' antioxidant capacity.
• Conflicting/paradoxical data from mortality endpoint studies, particularly in the elderly, may be the result of ischemic preconditioning.
“Sleep Apnea” was RDI (AHI not defined) > 10, in men with symptoms. Lavie P Eur Respir J 2005, n=14589
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Research opportunities
Knowledge Gap #1: Do We Need to Treat Mild/Moderate Sleep Apnea in Older People?
Knowledge Gap #2: What IS sleep apnea?
CMS’s Definition of Obstructive Sleep Apnea (OSA)

CPAP will be covered for adults with sleep-disordered breathing if:

AHI ≥ 15  OR  AHI ≥ 5 with

- Hypertension
- Stroke
- Sleepiness
- Ischemic heart disease
- Insomnia
- Mood disorders
Decrease in airflow or chest wall movement to an amplitude smaller than approximately 25% (apnea) or 70% (hypopnea) of baseline for at least 10 seconds PLUS oxyhemoglobin desaturation of 4% or greater as compared with baseline.

Why? Impossible to get inter-scorer reliability otherwise.
SHHS’s AHI is really an ODI 4

All events (apneas and hypopneas) required a 4% oxygen desaturation to be counted because it was not otherwise possible to achieve acceptable inter-rater reliability based on flow rate or arousals.
Scoring Apneas and Hypopneas
According to the AASM Scoring Manual
(Iber C, AASM, 2007)

Apneas are measured with a thermistor
  Signal drops by 90% of baseline
  For at least 10 seconds
  No requirement for desaturation

Hypopneas are measured with a pressure transducer
  Signal drops by ≥ 30% of baseline with a ≥ 4% desat OR
  Signal drops by ≥ 50% of baseline with a ≥ 3% desat or the event is associated with an arousal.
What IS Sleep Apnea in Older People?

1/3 of seniors have AHI > 5, and most have symptoms (Phillips B Chest 1992, Ancoli-Israel Sleep, 1991)
Latest, Greatest Scoring Rules (JCSM 2012)

Apnea = signal drop ≥ 90% of pre-event baseline using an oronasal thermal sensor, PAP device flow or an alternative apnea sensor for ≥ 10 seconds.

Hypopnea = signal drop by ≥ 30% of pre-event baseline for > 10 seconds in association with either ≥ 3% arterial oxygen desaturation or an arousal.
Severity Criteria Based on PSG From the American Academy of Sleep Medicine (Sleep, 1999)

“Mild” sleep apnea is 5-15 events/hr

“Moderate” sleep apnea is 15-30 events/hr

“Severe” sleep apnea is over 30 events/hr

(“Events” includes apneas, hypopneas, and RERA’s)

This gives no importance to symptoms, hypoxemia, sleep disturbance.
Which Patient Has “Mild” OSA?

<table>
<thead>
<tr>
<th></th>
<th>Patient 1</th>
<th>Patient 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>AHI (events/hr)</td>
<td>40</td>
<td>10</td>
</tr>
<tr>
<td>Apnea duration (secs)</td>
<td>10-22</td>
<td>10-90</td>
</tr>
<tr>
<td>Lowest SaO2 (%)</td>
<td>90</td>
<td>71</td>
</tr>
<tr>
<td>% REM on study</td>
<td>18</td>
<td>0</td>
</tr>
<tr>
<td>Arousals/hr</td>
<td>8</td>
<td>80</td>
</tr>
<tr>
<td>Cardiac arrhythmias</td>
<td>none</td>
<td>v tach</td>
</tr>
</tbody>
</table>
Do Symptoms and Definitions Matter? (Sforza E, Sleep Med 2015, n=825, mean age 68 yrs)

- Population-based cohort study (PROOF) in France
- “Sleepiness” defined by ESS > 10
- “Apnea” defined as >10 secs no flow
- “Hypopnea” > 10 secs 50% reduced flow, + 3% desat
- “Sleep apnea” defined solely on basis of AHI
  - < 5 normal
  - 5-15 mild
  - 15-30 moderate
  - >30 severe
- Mean ESS< 10 in all categories, ranging 5.7-6.6
- Desaturation was mostly mild (high 80s)
- Sleepiness correlated with AHI, ODI, min Sa02, T<90%, but male gender, depression and obesity were STRONGER predictors (confirmed by Lopes JM Rev Bras Epidemiol 2013, n=168 mean age 72)
- The authors propose two key concepts:
  - Older patients with OSA are a different phenotype
  - Identification/management of OSA in older patients is not clear cut
Knowledge Gap #3: How (And When) Should We Treat CENTRAL Apnea?
CANADIAN POSITIVE AIRWAY PRESSURE TRIAL FOR TREATMENT OF CENTRAL SLEEP APNEA IN HEART FAILURE

- 5 Year, multi-center RCT to examine effects of treating CSA by CPAP in patients with CHF
- Jointly funded by the CIHR, Respironics, ResMed and Tyco
“Adaptive servo-ventilation had no significant effect on the primary end point inpatients who had heart failure with reduced ejection fraction and predominantly central sleep apnea, but all-cause and cardiovascular mortality were both increased with this therapy.”
Overview
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Knowledge Gaps

- What IS sleep apnea (OSA) in the elderly?
  - Is it different than OSA in younger people? How?
- How is it best defined:
  - AHI, RDI, ODI, T<90%?
  - Symptoms?
- Is intermittent hypoxia a threat or a menace? And…
  - Are some older people better off not being treated?
- What treatments are most effective for central sleep apnea?
  - Or when does it need to be treated?
Summary/Key Questions

What IS sleep apnea in the older person, and how should it best be defined and measured?

Is intermittent hypoxemia a friend or a foe?

HOW (and WHEN) do we treat central sleep apnea?