Define common outcome metrics in OSA
Al-Shawwa Sleep Med Rev 2008

Redefining successful therapy in OSA:
A call to arms
Pang Laryngoscope 2014

Outcome measurements on OSA:
Beyond the AHI
Tam Laryngoscope 2014

Effects of Sleep Disordered Breathing (SDB)

- Physiologic
  - Increased incidence of MI, CVA, H/T
- Behavioral / Cognitive
  - Daytime sleepiness, increased MVA incidence up to 7x
  - MVA risk in men evident with snoring alone w/o OSA Young 1997
- Social
  - Snoring, disruption of marital harmony
What metrics are available?

- Cardiovascular morbidity
- Cognitive function / motor vehicle accidents
- Other physiologic / metabolic parameters
- Snoring (after all, that’s what brings them in, and that’s what patients judge treatment by)
- PSG

Cardiovascular Disease (SHHS)

- Heart failure, stroke
  - Shahar 2001
- Right Heart Function
  - Dursunoglu 2006
- Ischemic changes in the brain
  - Ding 2004
    - Arousals, not AHI
- Association with Hypertension
  - Could not correlate with PSG parameter
  - Redline 2005
  - Higher incidence of HT in sleepy patients
    - Kapur 2008

Cardiovascular disease (SHHS) cont.

- Carotid plaques
  - No association with AHI
  - Also looked at degree of hypoxemia and freq of arousals
  - All differences explained by confounding factors (for CVD)

- Is there NO association of carotid plaques with SDB, or just not with these parameters?
  - Wattanakit 2007

How about snoring???

Cardiovascular disease and snoring

- 54 patients with snoring and AHI <5
- Carotid artery intima-media thickness associated with snoring in pts without OSA
  - Deeb Laryn 2014
Neurophysiologic Effects - testing

- Attention is impaired
  - PVT (reliable, no learning, sensitive) Balkin 2004

- Vigilance and cognitive functioning impaired
  - Intellectual and verbal functioning relatively spared
  - These improve with treatment (CPAP) Beebe 2003

- Cognitive function testing does not correlate w/ AHI Boland 2002 (SHHS)

Cognitive Function - patient report measures

- Epworth Sleepiness Scale Johns 1991
  - 0-24 scale for “chance of dozing”
  - Average if 7 for medical students, 14 for OSA patient

- Functional Outcomes of Sleep Questionnaire (FOSQ) Weaver 1997
  - Measures impact of sleepiness on functioning

- Calgary Sleep Apnea Quality of Life Index Flemons 1997
  - Captures QOL, performance, mood

- Stanford Sleepiness Scale Hoddes 1973
  - Measure of sleepiness on a 1-7 scale meant to be used at different times during the day for comparison

Metabolic measures?

- Inflammatory
  - Elevated IL-6, TNF-alpha, CRP O2 radicals Schultz 2000 Teramoto 2003

- Hormonal changes
  - fT4, testosterone, LH, SHBG Meston 2003

- Diabetes, ILGF-1, sympathetic tone

- Ischemic changes in the brainstem
  - related to arousals, but not apnea or hypopnea Ding 2004

Will these measures ultimately be what we follow to determine treatment effectiveness? For diagnosis? HbA1c for OSA?

Metabolic Changes with Treatment

- CRP decreases in responders to multilevel surgery n=30
  - Level decreased a mean of 1.02 mg/l
  - Improvements in HRQL in responders and non-responders
  - No change in 17 non-responders Kezirian 2010

- CRP decreases in compliant CPAP users n=20
  - Level decreased a mean of 1.4 mg/l
  - Endothelial function improved as well Panoussopoulos 2012
  - No change in 6 non-compliant patients
Snoring

• Subjective spouse measures
  – Surrogate measure with VAS, "bother scale", etc

• Objective sound measurements
  – difficult, but possible, to quantify

• SNAP frequency analysis
  – analyzes snoring frequency and amplitude algorithm proprietary
    Liesching 2004

Snoring and CV Outcomes

• Self reported snoring in 42,244 women (WHI)
  – Snoring associated with modest risk for CHD, CVA, CVD
    Sands 2013

• Snoring studied as risk factor for CV risk/mortality n=380
  – Studied over 17 years
  – Snoring not associated with death, CV risk unadjusted or models
    adjusted for OSA
    Marshall 2012

Polysomnography Measures

• Multiple measures possible, a few are popular
  – Apnea Hypopnea Index (AHI)
  – Respiratory Disturbance Index (RDI)
  – Minimum O2 Saturation
  – Arousals
  – Time in REM sleep
  – Total apnea time
  – Total sleep time below 90% saturation

Does a polysomnogram alone define this disease?

Definitions of Disease

• Sleep Disordered Breathing - Recurrent episodes of cessation of respiration (apnea) or decrements in air flow (hypopnea) which may disrupt sleep
Definition of Apneic Events on PSG

- **Apnea** - Cessation of breathing during sleep for >10 sec
- **Hypopnea** - Decrease in air flow of >50% associated with a fall in SaO2 >4% +/- EEG arousal
- **Apnea Hypopnea Index (AHI)** - The number of apneas + hypopneas per hour of sleep; add RERAs/hour to get the Respiratory Disturbance Index (RDI)

Definitions of Disease by PSG

- **Obstructive Sleep Apnea** (25% males, 9% females, Young 1993)
  - AHI >5 events/hour

- **Obstructive Sleep Apnea Syndrome** (4% m, 2% f, Young 1993)
  - AHI >5 events/hour with symptoms (eg. daytime sleepiness)

- **Upper Airway Resistance Syndrome**
  - Repeated arousals 2° to upper airway resistance or snoring

What level of disease on PSG justifies treatment?

- Is there an AHI cut off?
  - Elevated AHI with no sleepiness, hypertension or co-morbidity?
  - Tiredness with a ‘normal’ AHI?
  - Desaturation only?

- How about length of apneas and hypopneas?

- Other parameters? REM, delta sleep, >90% sat

Polysomnography measures

- How well do PSG measures correlate with other measures?

- Weaver 2005
  - Analyze PSG/non-PSG measures in mild-moderate OSAS
  - FOSQ, SNORE, SF-36, ESS, PVT
  - No significant association between AHI and any baseline or outcomes non-PSG measure
  - Conclusion: PSG measures do not capture all elements of OSAS and should not be used exclusively to evaluate treatment response
What should the definition of hypopnea be?

- Should it be based on what correlates with cardiovascular disease? Punjabi 2008
- Hypopneas comprise a majority of SDB events
- Controversy exists with regard to definition
- In sample of 6,106 patients, hypopneas with a desaturation of at least 4% are associated with CVD
- There was NO correlation with milder desaturations or arousals

PSG and Tiredness from Sleep Heart Health Study

- Analysis of 1115 patients in the SHHS Kapur 2005
- AHI > 15 45.7% of patients with were sleepy
- AHI > 30 51.4% of patients with were sleepy
- AHI did correlate with sleepiness (p< .01)
- Sleepy patients
  - AHI 31.6
- Statistically significant, but clinically significant?
  - Not very discriminating for the clinician

Is Tiredness Important??

- Does self reported sleepiness by ESS modify the association between sleep apnea and hypertension? Yes! Kapur 2008
- Odds ratio for H/T if sleepy 2.83
- Odds ratio for H/T if NOT sleepy 1.22

Consensus Statement on Treatment Criteria in OSA

Daniel I. Loube, MD, FCCP; Peter C. Gay, MD, FCCP
Kingman P. Strohl, MD, FCCP; Allan I. Pack, MD, PhD
David P. White, MD, FCCP; Nancy A. Collop, MD, FCCP

CHEST 1999; 115:863–866

CPAP treatment

- All patients with an RDI>30, regardless of symptoms
- For patients with an RDI of 5 to 30 w/ symptoms or co-morbidities excessive daytime sleepiness, impaired cognition, mood disorders, insomnia, or documented cardiovascular diseases to include hypertension, ischemic heart disease, or stroke
Treatment Guidelines

“In the majority of patients without coexisting conditions…the primary reason to test for and treat sleep apnea is the potential to improve the quality of life”

Flemons NEJM 2002

Treatment Guidelines (cont)

“Clinicians do not make decisions about treatment on the basis of AHI alone because it correlates poorly with QOL and the severity of symptoms and does not help to determine the risk of MVA.”

Flemons NEJM 2002

Clinical Guideline for the Evaluation, Management and Long-term Care of OSA in Adults

Lawrence J. Epstein, M.D.  David Kristo, M.D.
Patrick J. Strollo, Jr., M.D.  Norman Friedman, M.D.
Atul Malhotra, M.D.  Susheel P. Patil, M.D., Ph.D.
Kannan Ramar, M.D.  Robert Rogers, D.M.D.
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Edward M. Weaver, M.D., M.P.H.


Diagnosis of OSA is confirmed if the number of obstructive events (apneas, hypopneas + RERA) > 15 events/hr or > 5/hour in a patient with symptoms

PAP is the treatment of choice for mild, moderate, and severe OSA and should be offered as an option to all patients. Alternative therapies may be offered depending on the severity of the OSA

Conclusions

• The proper metric or groups of metrics to measure this disease and guide our treatment is unclear
  – PSG alone does not appear to fully describe the disease

• It is likely that measures of physiology (tiredness, CV morbidities, serology) are what we should ultimately treat, not a number on the PSG

• Metrics should reflect what is important to the doctor (CV morbidity, MVA) AND the patient (how do I feel)?

• We should strive to define the physiology more completely and develop more robust metrics to define sleep disordered breathing