Outcome Measures in OSA
Defining Our Treatment Goal

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Overview

- What are the effects of SDB?
- What changes do our treatments make?
- What metrics are available?
- What metrics should we follow?
- Conclusions
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 w/ 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

• Ischemic changes in the brain
  Ding 2004
  – Arousals, not AHI

• Association with Hypertension
  Redline 2005
  – Could not correlate a specific parameter of PSG

• Right Heart Function
  Dursunoglu 2006

http://www.jhucct.com/shhs/
Cardiovascular disease (SHHS) cont.

• Carotid plaques
  – No association with RDI (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 OSA, or just not with these parameters?

  Wattanakit 2007
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
  - O2 radicals  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?**
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
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 $2^0$ to upper airway resistance or snoring
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
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
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

Where is sleepiness in the definition of SDB???
Treatment “Effectiveness”

- Haraldsson tested patients with SDB and normals on a driving simulator (at the Saab factory)
- Performed UP3 on patients with SDB
- Found that patients w/ SDB uniformly improved after UP3 REGARDLESS OF CHANGES IN AHI
- Did these patients with improved alertness and no change in AHI FAIL treatment? Haraldsson 1995
What metric describes the PHYSIOLOGY of the disease?

- PSG?
- Cardiovascular effects (H/T, MI, CAD)
- Sleepiness testing (MSLT, MWT, PVT)
- Endocrine/metabolic effects (CRP, sympathetic tone, IL-6)

- Are the physiologic changes that cause cardiovascular effects the same as the physiologic changes that cause sleepiness or metabolic effects?
Is there one metric for everyone?

One physiologic measurement may not be sufficient
- like measuring blood lipids (Total Chol, HDL, LDL)

There is undoubtedly differential susceptibility in their physiologic measures, just as there are for patients with sleep deprivation and many other diseases
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
“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
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
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.
Richard J. Schwab, M.D.           Michael D. Weinstein,
M.D.          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
Outcomes Measures in Obstructive Sleep Apnea

References


