Sleep Disordered Breathing in Heart Failure
When and How to Treat

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Disclosures

• ResMed – honorarium and travel reimbursement
• Peter C. Farrell USCD Sleep Center of Excellence
• Itamar, LLC – honorarium and travel reimbursement
• Novartis – Study Steering Committee
Outline

• Quick Review of Obstructive Sleep Apnea (OSA)
  • Epidemiology
  • Pathophysiology
  • Treatment

• Obstructive Sleep Apnea and Heart Failure

• Central Sleep Apnea and Heart Failure
Take Home Messages

• OSA is very common in heart failure patients

• Treatment of OSA can improve blood pressure and cardiovascular function (modestly), but may also improve other symptoms

• Adherence is likely to be key

• Cheyne Stokes Respiration in heart failure is an ominous sign
Patterns of Apnea

Obstructive

Airflow

Respiratory effort

Central
Upper Airway Collapse

Arousal from sleep

Oxygen desaturation
Repetitive collapse, desaturation, arousal

OSA severity = (apnea + hypopneas)/total sleep time
= Apnea-hypopnea index (AHI)

- AHI < 5 events/hr  Normal
- AHI > 5 – 15       Mild
- AHI > 15 – 30      Moderate
- AHI > 30           Severe
Prevalence

30-60 year olds

Percent of Population

Sleep apnea Syndrome

= AHI >5/hr + symptoms

Adapted from Young T et al. *NEJM* 1993
BMI >30 in US Adults

2014 Estimate of moderate and severe OSA:
17% of middle aged men
9% of middle aged women

Source: Behavioral Risk Factor Surveillance System, CDC
HypnoLaus study

• Population based study in Lausanne, Switzerland

• PSGs performed in more than 2,000 people chosen at random, ages 40-80 years old

• 23% of women had moderate to severe OSA (AHI > 15 events/hour)

• 50% of men had moderate to severe OSA

• Mean BMI = 25.6 kg/m2

Heinzer Lancet Resp Med 2015
Pathophysiology
Thoracic pressure swings (↑LV afterload)

Cardiovascular sequelae
- ↑Endothelin
- ↓Vagus

Compensatory negative pressure reflex
- ↑Activity of pharyngeal dilators (genioglossus)

Maintains upper airway patency
- Sleep fragmentation
- Arousal

Neurocognitive sequelae
- Loss of negative pressure reflex
- ↓Activity of pharyngeal dilators
- Hypoxia and hypercapnia

Airway collapse
Consequences

**Neurocognitive**
- Excessive daytime sleepiness
- Increased motor vehicle crashes
- Increased work-related accidents
- Poor job performance
- Decreased quality of life

**Cardiovascular**
- Systemic hypertension
- Cardiac arrhythmias
- Myocardial ischemia
- Cerebrovascular disease
- Pulmonary Hypertension/ cor pulmonale
OSA and Hypertension

Dog Model of Apnea (Brooks et al, JCI 99:106, 1997)
OSA and changes in nocturnal blood pressure
OSA and changes in daytime blood pressure

[Graph showing changes in daytime blood pressure with sleep apnea and sleep fragmentation markers.]

- Black square: Sleep apnea
- White circle: Sleep fragmentation
Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: an observational study


MI or stroke

Cumulative incidence of fatal CVS events (%)

- Controls
- Snorers
- Mild OSAH
- Severe OSAH
- OSAH with CPAP
Treatment of OSA

• Behavioral

• Medical/Device

• Surgical
Weight loss and OSA severity

![Bar chart showing changes in AHI, Events/hr with change in body weight.

Mean Change in AHI, Events/hr

-20 to -10% to -5% to +5% to +10% to +20

Change in Body Weight

Adapted from Peppard JAMA 2000
Medical/Device Therapy

• Positive airway pressure – works if tolerated

• Devices – variable efficacy
  • Oral appliances
  • Expiratory resistance valves
  • Hypoglossal nerve stimulator
  • Suction devices
Positive Airway Pressure
Steady Improvements in Acceptability

Interfaces

Auto-titrating PAP
Steady Improvements in Acceptability Monitoring

Usage

- 5:45 usage hours: 61 / 70
- Good mask seal: 7 / 10
- 2.4 events per/hr: 9 / 10
- 2 mask on/off events: 8 / 10
- Your myAir score is: 85 / 100
Who to treat with CPAP?

• Can always do a therapeutic trial

• Those with symptoms

• Those with severe medical co-morbidities

• Those with severe disease (by AHI or substantial oxygen desaturations)
Hypoglossal Nerve Stimulator therapy
Effect of OSA treatment on blood pressure

Montesi JCSM 2012
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Prevalence and Predictors of Sleep-Disordered Breathing in Patients With Stable Chronic Heart Failure

The SchlaHF Registry

Michael Arzt, MD, Holger Woehrle, MD, Olaf Oldenburg, MD, Andrea Graml, Dipl Stat, Anna Suling, PhD, Erland Erdmann, MD, Helmut Teschler, MD, Karl Wegscheider, PhD for the SchlaHF Investigators

NYHA II and above, LVEF ≤45%
6,876 patients
Prevalence of SDB (AHI ≥15/h) in patients with chronic heart failure by age and sex, adjusted for all other risk factors in the model. Abbreviations as in Figure 1.
Prevalence of SDB (AHI ≥15/h) in patients with chronic heart failure by BMI (A) and LVEF intervals (B), adjusted for all other risk factors in the model. Abbreviations as in Figures 1 and 2.
High Prevalence of Sleep Apnea in Heart Failure Outpatients: Even in Patients With Preserved Systolic Function

TOBIAS E. HERRSCHER, MD, HARRIET AKRE, MD, PhD, BRITT ØVERLAND, PhD, LEIV SANDVIK, PhD, AND ARNE S. WESTHEIM, MD, PhD

SDB in patients with reduced and preserved ejection fraction

J Card Failure 2011
Treatment of OSA in HF *should* help

- Decrease arousals from sleep – reduce catecholamines

- Decrease LV afterload – thoracic pressure swings minimized
  - BP better
CPAP treatment reduces catecholamines
CPAP treatment can reduce afterload

Left Ventricular Intracavitary Pressure = 100 mmHg

Thoracic Pressure = 0 mmHg

LV transmural pressure (work) = 100 - 0 = 100 mmHg

No upper airway obstruction

To aorta (100 mmHg)
CPAP treatment can reduce afterload

Left Ventricular Intracavitary Pressure = 120 mmHg
Thoracic Pressure = -20 mmHg
LV transmural pressure = 100 - (-20) = 120 mmHg
CPAP improves LVEF

Kaneko *NEJM* 2003
Sleep Apnea Testing and Outcomes in a Large Cohort of Medicare Beneficiaries with Newly Diagnosed Heart Failure

Shahrokh Javaheri¹, E. Ben Caref², Er Chen³, Kuo Bianchini Tong³, and William T. Abraham⁴

Figure 2. Kaplan-Meier survival curves for the tested, diagnosed, and treated subjects versus not tested and not treated subjects, adjusted by age, sex, and Charlson Comorbidity Index, 2004 through 2005. CI = confidence interval; HF = heart failure.
CPAP for Prevention of Cardiovascular Events in Obstructive Sleep Apnea

R. Doug McEvoy, M.D., Nick A. Antic, M.D., Ph.D., Emma Heeley, Ph.D., Yuanming Luo, M.D., Qiong Ou, M.D., Xilong Zhang, M.D., Olga Mediano, M.D., Rui Chen, M.D., Luciano F. Drager, M.D., Ph.D., Zhihong Liu, M.D., Ph.D., Guofang Chen, M.D., Baoliang Du, M.D., Nigel McArdle, M.D., Sutapa Mukherjee, M.D., Ph.D., Manjari Tripathi, M.D., Laurent Billot, M.Sc., Qiang Li, M.Biostat., Geraldo Lorenzi-Filho, M.D., Ferran Barbe, M.D., Susan Redline, M.D., M.P.H., Jiguang Wang, M.D., Ph.D., Hisatomi Arima, M.D., Ph.D., Bruce Neal, M.D., Ph.D., David P. White, M.D., Ron R. Grunstein, M.D., Ph.D., Nanshan Zhong, M.D., and Craig S. Anderson, M.D., Ph.D., for the SAVE Investigators and Coordinators*
Secondary prevention study in moderate/severe OSA

METHODS
After a 1-week run-in period during which the participants used sham CPAP, we randomly assigned 2717 eligible adults between 45 and 75 years of age who had moderate-to-severe obstructive sleep apnea and coronary or cerebrovascular disease to receive CPAP treatment plus usual care (CPAP group) or usual care alone (usual-care group). The primary composite end point was death from cardiovascular causes, myocardial infarction, stroke, or hospitalization for unstable angina, heart failure, or transient ischemic attack. Secondary end points included other cardiovascular outcomes, health-related quality of life, snoring symptoms, daytime sleepiness, and mood.
Why?
Adherence = 3.3 h/night

Is it too late?

Peker AJRCCM 2016
“RICCADA”
- non sleepy OSA
- improved outcomes, if used
Who to treat with CPAP in HF?

• Can always do a therapeutic trial

• Those with symptoms (consistent signal here)

• Those with severe medical co-morbidities

• Those with severe disease (by AHI or substantial oxygen desaturations) – but they need to use it
Effect of Early Intervention With Positive Airway Pressure Therapy for Sleep Disordered Breathing on Six-Month Readmission Rates in Hospitalized Patients With Heart Failure

Sunil Sharma, MD\textsuperscript{a,*}, Paul Mather, MD\textsuperscript{b}, Ankit Gupta, MD\textsuperscript{a}, Gordon Reeves, MD\textsuperscript{b}, Sharon Rubin, MD\textsuperscript{b}, Raphael Bonita, MD\textsuperscript{b}, Anindita Chowdhury, MD\textsuperscript{a}, Raymond Malloy, BS\textsuperscript{a}, Leslee Willes, MS\textsuperscript{c}, and David Whellan, MD\textsuperscript{b}

Am J Card 2016
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Patterns of Apnea

Obstructive

Central

Airflow

Respiratory effort
Crescendo-decresendo pattern

Arousals

Oxygen desaturation - reoxygenation
Epidemiology of CSR

• Occurs in both systolic and diastolic heart failure

• Prevalence remains high (~30%) in patients with stable CHF, even those on modern therapies

• Prevalence increases with increasing CHF severity

• Patients with CSR and CHF do worse than those without CSR

Javaheri S, Circ. 1998; 97(21) :2154-9
MacDonald M, JCSM. 2008; 4(1): 38-42
Khayat J Card Fail 2012
Khayat Eur Heart J
CSR Treatment

A

R=0.47
P=0.006

B

CSR Treatment

• Treat CHF
  • Improve cardiac function, left atrial pressure, and pulmonary congestion in order to decrease circulatory delay and lower chemosensitivity

• Supplemental oxygen therapy

• PAP therapy

• Respiratory stimulants to lower CO2

• Sedatives to facilitate sleep
Treatment of CSA in HF *should* help

- Reduce hypoxemia
- Decrease arousals from sleep – reduce catecholamines
- Decrease LV afterload – thoracic pressure swings minimized
Continuous Positive Airway Pressure for Central Sleep Apnea and Heart Failure

T. Douglas Bradley, M.D., Alexander G. Logan, M.D., R. John Kimoff, M.D., Frédéric Sériès, M.D., Debra Morrison, M.D., Kathleen Ferguson, M.D., Israel Belenkie, M.D., Michael Pfeifer, M.D., John Fleetham, M.D., Patrick Hanly, M.D., Mark Smilovitch, M.D., George Tomlinson, Ph.D., and John S. Floras, M.D., D. Phil., for the CANPAP Investigators*
CPAP improves LVEF
CPAP doesn’t improve survival...

![Graph showing survival rates with and without CPAP](image-url)
...Unless CPAP improves the AHI

Adaptive Servo Ventilation

Thoracic excursions

Abdominal excursions

Ventilatory airflow (L/s)

$\text{SpO}_2$ (%)

EKG

Ventilator support

Apnea phase

Hyperventilation phase

Circulatory delay

1 min
Adaptive Servo-Ventilation for Central Sleep Apnea in Systolic Heart Failure

Martin R. Cowie, M.D., Holger Woehrle, M.D., Karl Wegscheider, Ph.D., Christiane Angermann, M.D., Marie-Pia d’Ortho, M.D., Ph.D., Erland Erdmann, M.D., Patrick Levy, M.D., Ph.D., Anita K. Simonds, M.D., Virend K. Somers, M.D., Ph.D., Faiez Zannad, M.D., Ph.D., and Helmut Teschler, M.D.
A Primary End Point

Hazard ratio, 1.13 (95% CI, 0.97–1.31)
P = 0.10

Cumulative Probability of Event

Months since Randomization

No. at Risk

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Treatment of CSA in HF *should* help but doesn’t

• ASV Therapy is **directly** harmful?
  • Changes in thoracic pressure with PAP – decreased preload?
  • Changes in pCO2 level

• ASV Therapy **indirectly** led to changes in other medications/activity level

**N.B. ASV still indicated for treatment of other central apneas**
Take Home Messages

• OSA is very common in heart failure patients

• Treatment of OSA can improve blood pressure (modestly), but may also improve other symptoms

• Adherence is likely to be key

• Cheyne Stokes Respiration in heart failure is still an ominous sign
  • Best therapy is to optimize heart failure
Thank you

• rowens@ucsd.edu
Day–Night Pattern of Sudden Death in Obstructive Sleep Apnea

Apoor S. Gami, M.D., Daniel E. Howard, B.S., Eric J. Olson, M.D., and Virend K. Somers, M.D., Ph.D.
Atrial Fibrillation and OSA

Fein JACC 2013
Pulmonary Hypertension

Sajkov AJRCCM 1999, 2002