Heart Failure and Sleep Apnea

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- I have no relationships to disclose

"But the tigers come at night,
With their voices soft as thunder,
As they tear your hope apart,
As they turn your dream to shame."

From "I Dreamed a Dream," *Les Miserables*

Kryger et al. In: *Principles and practice of sleep medicine.* W.B. Saunders Company; 2000.

Disclosures

- None

Sleep Apnea and Heart Failure

- Sleep Archictecture
- Diagnosis
- Treatment

Normal sleep

- What is REM sleep?
- What is NREM sleep?
- Predominant physiological processes that are different from wakefulness?

REM

- Low voltage cortical EEG
- REM
- Muscle atonia
- Vivid dreams
- Spontaneous waking occurs most often
- Difficult to wake someone up

REM

- Irregular breathing patterns
- Increased threshold for a ventilatory response
- Reduction in ventilatory responsiveness to chemostimulation
- Skeletal muscle atonia
- Increases in pCO2

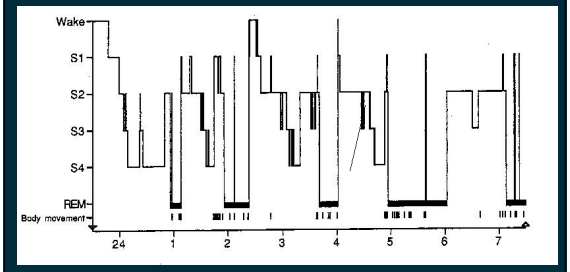
REM

Stages 1-4 NREM

- Decrease in central respiratory drive
- Increase in CO2
- Sleep is under metabolic control
- Parasympathetic tone increases
- Sympathetic tone decreases
- Heart rate, blood pressure, stroke volume decrease

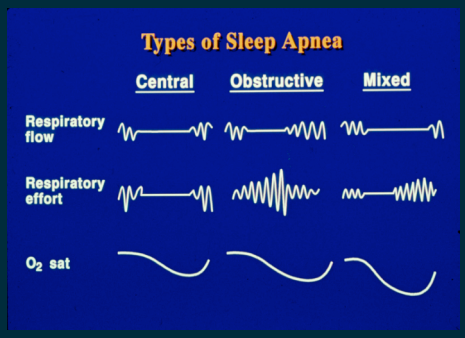
Intermittent Arousals

- Reinstitution of wakefulness drive to breathe
- Augmented ventilation
- Abrupt increases in HR and BP
- Increases in SNA
- Therefore, arousal in a distinct transient state of heightened respiratory and cardiovascular activity



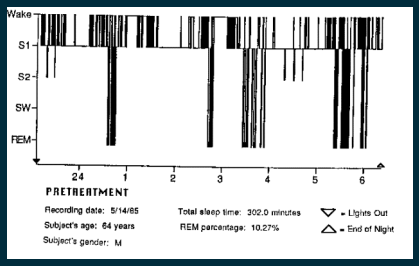
Physiology of Normal Sleep

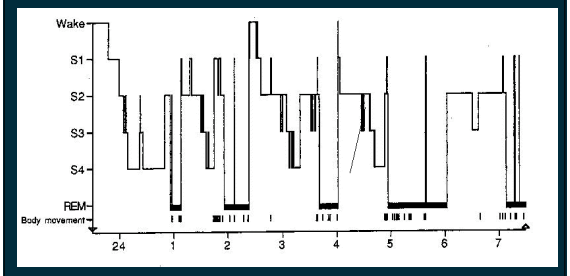
- Wakefulness to NREM sleep
- Withdrawl of nonchemical wakefulness drive to breathe
- Minute ventilation decreases
- CO2 increases



Definitions

- Apnea-Complete cessation of airflow for at least 10 seconds
- Hypopnea-Decrease in oronasal airflow by at least 50% associated with a 4% decrease in arterial saturation
- AHI-Apnea Hypopnea index. Combined episodes per hour.





Clinical Diagnosis

- Symptoms of daytime somnolence, snoring, witnessed apneas, generalized poor sleep.
- Questionnaires such as the Berlin questionnaire

Prevalence of Sleep Apnea and Heart Failure

- Sleep apnea—10% prevalence in the general population
- Heart failure—2% prevalence
- 11%-38% had OSA
- 33%-42% had CSA

Arzt & Bradley. *Am J Respir Crit Care Med.* 2006;173:1300.

Question # 1

Which one of the following is true:

A. Central sleep apnea decreases sympathetic tone

B. Central sleep apnea increases negative intrathoracic pressure

C. Heart failure often leads to a decreased CO_2

D. Elevated CO_2 leads to Cheyne-Stokes respirations in patients with HF

Obstructive Sleep Apnea Can Cause Heart Failure

- Increased afterload due to negative intrathoracic pressure
- Hypoxia
- Increased sympathetic tone
- Increased catecholamines
- Vascular endothelial dysfunction

Arzt & Bradley. *Am J Respir Crit Care Med.* 2006;173:1300.

Can Central Sleep Apnea Exacerbate Heart Failure?

- Hypoxia
- Increased sympathetic tone
- Increases in heart rate
- Increases in blood pressure
- Arrhythmias

Bradley & Floras. *Circulation.2003;107:1822.*

Normal Hemodynamic Values

- RA 5-8 mmHg
- RV 25/5 mmHg
- PA 25/10 mmHg
- PCWP 10 mmHg
- CI 2.5-3.5 l/min/m2

Case Study

- 75 year old man with long history of an LVEF of <20%
- Fatigued walking 2-3 blocks
- Very poor sleep over 2 weeks. No orthopnea or PND
- Exam: SBP=80, HR 90, Clear lungs, + JVD, + S3, No edema, BNP 2400
- Hemodynamics?

Hemodynamics

- RA 13mmHg
- RV 60/20mmHg
- PA 60/30mmHg
- PCWP 30mmHg
- CI 1.4 l/min/m2

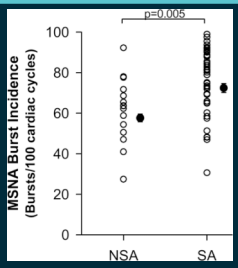
How CHF May Induce Central Sleep Apnea

- Elevated PCWP causes hyperventilation through pulmonary vagal irritant receptors
- CO_2 decreases
- Triggers apneas

Solin et al. *Circulation.* 1999;99:1574.

PCWP = pulmonary capillary wedge pressure

CSA May Aggravate Cardiac Function by Increasing SNS Tone



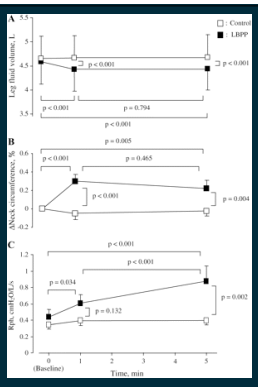
Spaak et al. *Hypertension.* 2005;46:1327.

SNS = sympathetic nervous system

CHF May Lead to OSA

- Increased filling pressures can result in pharyngeal edema, which can reduce cross-sectional area in the airway

Shepard, Jr. et al. *Am J Respir Crit Care Med.* 1996;153:250.



Changes in leg fluid, neck circumference, and pharyngeal resistance in response to lower body positive pressure.

Chiu et al. *Am J Respir Crit Care Med.* 2006;174:1378.

Question #2

- In patients with heart failure who have both OSA and CSA, CSA becomes more predominant as sleep progresses through the night.

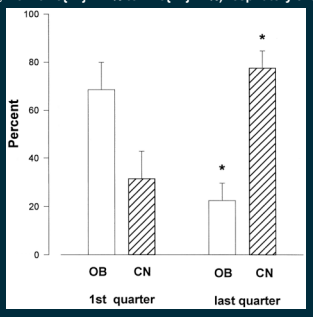
A. True
B. False

Overnight Shift from OSA to CSA

- In cases where OSA and CSA are both present, CSA increases throughout the night
- CO2 decreases

Tkacova et al. Circulation.2001;103;238

From first to last quarter of night, there was significant reduction in proportion of obstructive (OB; from 68.5{+/-}11.4% to 22.5{+/-}7.2%) and increase in proportion of central (CN; from 31.5{+/-}11.4% to 77.5{+/-}7.2%) respiratory events

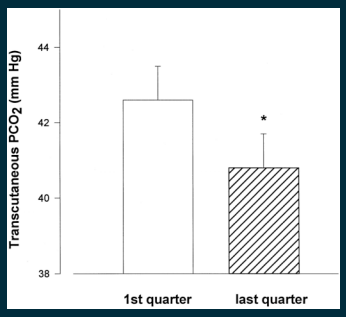


Tkacova, R. et al. Circulation 2001;103:238-243

Circulation

American Heart Association. Learn and Live.

PtcCO2 decreased from 42.6{+/-}0.9 mm Hg during first quarter to 40.8{+/-}0.9 mm Hg during last quarter of night

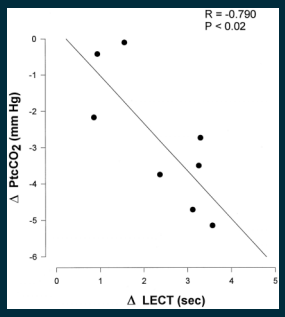


Tkacova, R. et al. Circulation 2001;103:238-243

Circulation

American Heart Association. Learn and Live.

Inverse relationship between change in PtcCO2 and LECT from OSA to CSA in 8 patients whose SaO2 was measured by ear oximeter



Tkacova, R. et al. Circulation 2001;103:238-243

Circulation

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Overnight Shift from OSA to CSA-Proposed Associations

- Hypoxia
- Increased sympathetic tone
- Increased afterload
- Increase venous congestion in recumbent position
- DETERIORATION OF VENTRICULAR FUNCTION

Tkacova et al. Circulation.2001;103;238

Clinical Diagnosis

- Symptoms of daytime somnolence, snoring, witnessed apneas, generalized poor sleep
- Questionnaires such as the Berlin Questionnaire
- Class III/IV Heart Failure

OSA: Treatment

- Positional changes
- Surgery—for extreme cases (large tonsils)
- CPAP
- BiPAP

BiPAP = bilevel positive airway pressure;
CPAP = continuous positive airway pressure

Surgical Interventions for OSA

- Uvuloplasty
- Laser-assisted uvuloplasty
- Radiofrequency volumetric tissue reduction
- Maxillary mandibular osteotomy
- Hyoid suspension
- Gastric reduction or bypass
- Tracheostomy

Hudgel. *Chest.* 1996;109:1346.

Treatment of OSA in HF

CPAP can treat OSA by

- Treating hypoxia
- Reducing nocturnal heart rate
- Reducing blood pressure
- Reducing LV afterload
- Improving the neural control of blood pressure and heart rate by increasing baroreflex sensitivity

Arzt & Bradley. *Am J Respir Crit Care Med.* 2006;173:1300.

LV = left ventricular

CSA: Treatment

- Treat the heart failure
- Pharmacologic therapy
- CPAP/BiPAP/adaptive servoventilation
- Oxygen
- Pacing (?)
- CO_2 (?)

Arzt & Bradley. *Am J Respir Crit Care Med.* 2006;173:1300.

Heart Failure Treatment

- Diuretics
- ACE Inhibitor
- Beta Blocker
- Spironolactone
- When hemodynamic stability is unclear, consider a right heart catheterization

Theophylline

- Theophylline increases central respiratory drive and cardiac contractility
- In a small study in patients with HF and CSA, theophylline reduced AHIs, but did not improve LVEF
- Theophylline is not routinely recommended due to possibility of cardiac arrhythmias

Javaheri et al. *N Engl J Med.* 1996;335:562.

LVEF = left ventricular ejection fraction

Acetazolamide (Diamox®)

- The carbonic anhydrase inhibitor acetazolamide stimulates respiration by causing metabolic acidosis
- In a small study of HF and CSA, acetazolamide reduced the AHI (by 38%), daytime sleepiness, and fatigue
- Safety and efficacy remain to be demonstrated

Javaheri. *Am J Respir Crit Care Med.* 2006;173:234.

Positive Airway Pressure: Treatment Modalities

- **Continuous positive airway pressure (CPAP):** remains continuous throughout the night; prevents airway obstruction
- **Bilevel positive airway pressure (BiPAP):** separate inspiratory and expiratory pressure; may improve tolerance
- **Adaptive servoventilation (ASV):** reacts to breathing patterns to cause a more stable respiratory pattern

Treatment of CSA in HF With CPAP

- CPAP reduces LV transmural pressure by increasing intrathoracic pressure
- Reduces LV preload
- Effects on CSA have been inconsistent
- Better effects with gradual up-titration to 8 to 12.5 cm H_2O
- CPAP has more favorable effects on the heart when AHI is decreased

Arzt & Bradley. *Am J Respir Crit Care Med.* 2006;173:1300.

Question # 3

- The CANPAP trial showed a survival benefit in patients with systolic heart failure receiving CPAP

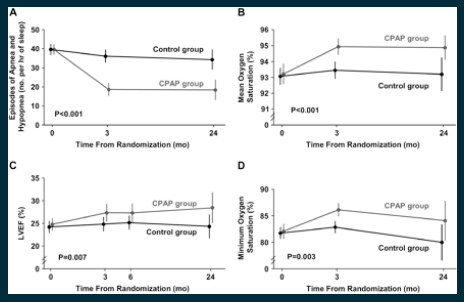
A. True
B. False

CANPAP Trial

- 258 patients with heart failure (mean LVEF = 24.5 ± 7.7%)
- 128 patients received CPAP
- 130 received no CPAP
- Endpoints were survival, EF, exercise capacity, quality of life, and neurohormonal responses

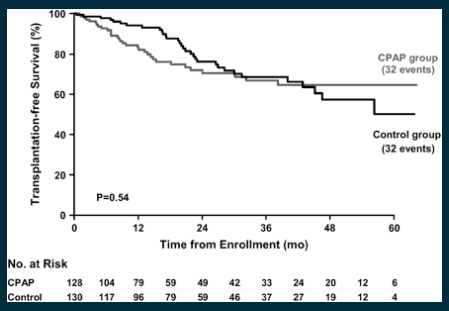
CANPAP = Canadian Positive Airway Pressure (trial); EF = ejection fraction

Bradley et al. *N Engl J Med.* 2005;353:2025.



Effect of CPAP on number of apneas and hypopneas per h of sleep (A), mean and minimum nocturnal oxygen saturation (B and D), and LVEF (C).

Arzt & Bradley. *Am J Respir Crit Care Med.* 2006;173:1300.



Transplantation-free survival rates for CPAP and control groups over time.

Bradley et al. *N Engl J Med.* 2005;353:2025.

CANPAP Results

- In patients with HF and sleep apnea, at 2 years there was no difference in survival without transplantation between those receiving and not receiving CPAP
- There were beneficial finding such as a decrease in the AHI and improvements in EF and neurohormones
- The clinical rate of events overall was less than expected leading to early cessation of the trial

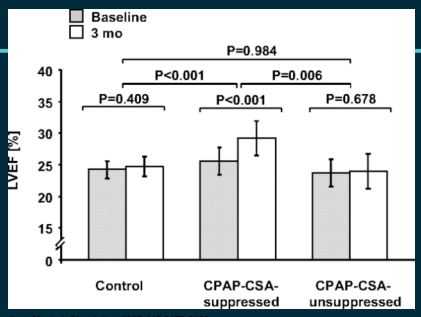
Bradley et al. *N Engl J Med.* 2005;353:2025.

CANPAP Revisited

- Post-hoc evaluation of patients who had early suppression of CSA (at 3 months)
- Two groups: CPAP suppressed group to AHI < 15 and non-suppressed group
- EF and transplant-free survival were improved in the group in which CPAP suppressed the AHI

Arzt, M. et al. Circulation 2007;115:3173-3180

Data shown are means (95% CI)



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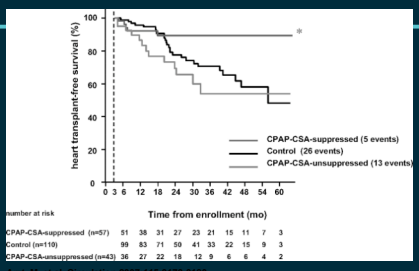
Kaplan-Meier survival plots demonstrating that compared with the control group, the CPAP-CSA-suppressed group had significantly improved heart transplant-free survival (*unadjusted P=0.043), whereas the CPAP-CSA-unsuppressed group did not (unadjusted P=0.260)



Arzt, M. et al. Circulation 2007;115:3173-3180

Circulation

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Adaptive Pressure Support Servoventilation: Right Pressures at the Right Time

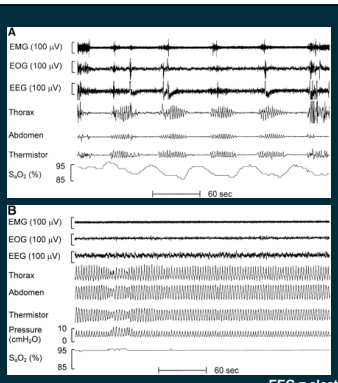
- Offers 4 to 5 cm H_2O expiratory support and 8 cm H_2O end-inspiratory pressure
- Can detect central apneas and increase inspiratory pressure to 15 cm H_2O
- Can overide central apneas
- Allows lower expiratory pressure support than CPAP

Teschler et al. *Am J Respir Crit Care Med.* 2001;164:614.

Adaptive Pressure Support Servoventilation (cont'd)

- 14 subjects with stable cardiac failure
- 4 treatment nights in random order during polysomnography:
  - Nasal oxygen (2 L/min)
  - CPAP (mean 9.25 cm H_2O)
  - BiPAP (mean 13.5/5.2 cm H_2O)
  - ASV largely at the default settings (mean pressure 7 to 9 cm H_2O)

Teschler et al. *Am J Respir Crit Care Med.* 2001;164:614.



Effects of adaptive servo-ventilation

EEG = electroencephalogram;
EMG = electromyogram;
EOG = electrooculogram

Teschler et al. *Am J Respir Crit Care Med.* 2001;164:614.

Improvements in AHI With Different Treatments

- AHI: declined from 44.5 ± 3.4/h (SEM) untreated to 28.2 ± 3.4/h with oxygen
- CPAP: 26.8 ± 4.6/h
- BiPAP: 14.8 ± 2.3/h
- ASV: 6.3 ± 0.9/h

Teschler et al. *Am J Respir Crit Care Med.* 2001;164:614.

Oxygen

- Can reduce AHI by 50%
- Decreases urine norepinephrine
- No effect on daytime plasma norepinephrine
- No effect on quality of life
- No effect on daytime sleepiness
- Does not predictably improve cardiac function

Arzt & Bradley. *Am J Respir Crit Care Med.* 2006;173:1300.

CPAP versus O_2

- Both decreased AHI by 67%
- CPAP improved ventilatory efficiency and LVEF; O_2 did not

Arzt et al. *Chest.* 2005;127:794.

Treatment with CO_2?

- Can obliterate CSA
- No evidence of positive outcomes
- Can increase sympathetic tone
- Not currently recommended

Khayat et al. *Chest.* 2003;123:1551; Lorenzi-Filho et al. *Am J Respir Crit Care Med.* 1999;159:1490.

Atrial Overdrive Pacing

- In patients with bradycardia, atrial overdrive pacing can decrease apneas and hypopneas
- These results have not been reproduced despite several attempts

Garrigue et al. *N Engl J Med.* 2002;346:404.

Biventricular Pacing and Obstructive Sleep Apnea

- 13 patients with HF and obstructive sleep apnea received CRT
- AHI decreased from 40.9 ± 6.4 to 29.5 ± 5.9 events per hour with CRT ($p = 0.04$).
- BL EF was 22 ± 1.7% and increased post-CRT to 33.6 ± 2.0% ($p < 0.05$).

Stanchina et al. Chest. 2007;132(2):433-439.

Biventricular Pacing and Obstructive Sleep Apnea

- The reduction in AHI with CRT correlated with a decrease in circulation time ($r = 0.89$; $p < 0.001$) with CRT.
- Increased pacing rate did not change AHI.
- CRT had no effect on sleep architecture or daytime symptom scores.

Stanchina et al. Chest. 2007;132(2):433-439.

Biventricular Pacing and Cheyne-Stokes

- 28 patients eligible for CRT underwent sleep studies after 6 months of CRT
- 12/28 patients had significant CSR (43%); 10 patients had a successful implantation and underwent repeat sleep study at 6 months
- 6/10 patients experienced a significant decrease in CSR severity following CRT.

Gabor et al. Eur espir J 2005;26:95-100.

Biventricular Pacing and Cheyne-Stokes

- Improvement in congestive heart failure-related hyperventilation and hypocapnia.
- No change in circulation time, oxygen saturation, frequency of obstructive apneas or sleep quality
- Conclusion: CRT is associated with a reduction in Cheyne-Stokes respiration

Gabor et al. Eur espir J 2005;26:95-100.

Biventricular Pacing and Central Sleep Apnea

- 24 patients EF 24 ± 6%, and LBBB (QRS duration 173 ± 22 ms) received a CRT device.
- 14 patients had CSA (AHI >5/h),
- 10 patients had an AHI <5/h without CSA.
- In patients with CSA, CRT decreased AHI (19.2 ± 10.3 to 4.6 ± 4.4, $p < 0.001$) PSQI (10.4 ± 1.6 to 3.9 ± 2.4, $p < 0.001$) and SaO_2 increased (84 ± 5% to 89 ± 2%, $p < 0.001$).

Sinha et al. J Am Coll Cardiol. 2004;44:68.

Biventricular Pacing and Central Sleep Apnea

- In patients without CSA, there was no significant change in AHI, PSQI, and SaO_2min.
- Conclusion: CRT decreases CSA and improves sleep quality in patients with HF and sleep-related breathing disorders.

Sinha et al. J Am Coll Cardiol. 2004;44:68.

Biventricular Pacing Conclusions

- Evidence to support improvement in OSA with biventricular pacing
- Evidence for a decrease in circulation time
- Improvements in CSA/CSR with biventricular pacing
- These findings support the role of HF in both CSA and OSA

Conclusion

- Use a low threshold when looking for sleep apnea in heart failure patients
- Both sleep apnea and heart failure can exert adverse effects on each other
- Aggressive intervention in the realms of both heart failure and sleep apnea is critical
- More study is required to identify best treatment patterns