Heart Failure and Sleep Apnea

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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

Sleep Apnea and Heart Failure

• Sleep Architecture
• 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
- 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
- Withdrawal 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

Obstructive Sleep Apnea Can Cause Heart Failure

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

Can Central Sleep Apnea Exacerbate Heart Failure?

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

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
- CO₂ decreases
- Triggers apneas

PCWP = pulmonary capillary wedge pressure

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CSA May Aggravate Cardiac Function by Increasing SNS Tone


SNS = sympathetic nervous system

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CHF May Lead to OSA

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


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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

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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

Clinical Diagnosis

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

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


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


PtcCO2 decreased from 42.6%(+/-)0.9 mm Hg during first quarter to 40.8%(+/-)0.9 mm Hg during last quarter of night


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
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


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


CSA: Treatment

- Treat the heart failure
- Pharmacologic therapy
- CPAP/BiPAP/adaptive servoventilation
- Oxygen
- Pacing (?)
- CO₂ (?)


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


LV = left ventricular
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


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 H₂O
- CPAP has more favorable effects on the heart when AHI is decreased


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


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).

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

**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 findings 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.

**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.

**Adaptive Pressure Support Servoventilation: Right Pressures at the Right Time**
- Offers 4 to 5 cm H₂O expiratory support and 8 cm H₂O end-inspiratory pressure.
- Can detect central apneas and increase inspiratory pressure to 15 cm H₂O.
- Can override central apneas.
- Allows lower expiratory pressure support than CPAP.

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**References**


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$_2$O)
  - BiPAP (mean 13.5/5.2 cm H$_2$O)
  - ASV largely at the default settings (mean pressure 7 to 9 cm H$_2$O)


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


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


CPAP versus O$_2$

- Both decreased AHI by 67%
- CPAP improved ventilatory efficiency and LVEF; O$_2$ did not


Treatment with CO$_2$?

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


EEG = electroencephalogram; EMG = electromyogram; EOG = electrooculogram
Atrial Overdrive Pacing

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


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).


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.


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.


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 SaO2 increased (84 ± 5% to 89 ± 2%, p < 0.001).

Biventricular Pacing and Central Sleep Apnea

- In patients without CSA, there was no significant change in AHI, PSQI, and SaO₂ min.
- Conclusion: CRT decreases CSA and improves sleep quality in patients with HF and sleep-related breathing disorders.


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