Central Sleep Apnea

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Disclosure

I, Vijay Bandhakavi, MD have no financial interests to disclose.
Objectives

Upon completion of this educational activity, the participant should be able to:

Objective 1: To name the causes of Central Sleep Apnea
Objective 2: To describe the pathophysiology of Central Sleep Apnea
Objective 3: To identify management options for Central Sleep apnea.
TREATMENT OF CENTRAL SLEEP APNEA SYNDROME IN ADULTS

The Treatment of Central Sleep Apnea Syndromes in Adults: Practice Parameters with an Evidence-Based Literature Review and Meta-Analyses

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The International Classification of Sleep Disorders, Second Edition (ICSD-2) distinguishes 5 subtypes of central sleep apnea syndromes (CSAS) in adults. Review of the literature suggests that there are two basic mechanisms that trigger central respiratory events: (1) post-hyperventilation central apnea, which may be triggered by a variety of clinical conditions, and (2) central apnea secondary to hypoventilation, which has been described with specific clinical disorders. The predominance of evidence in the treatment of CSAS supports the use of continuous positive airway pressure (CPAP). Much of the evidence comes from interventions on CSAS related to congestive heart failure (CHF), but other subtypes of CSAS appear to respond to CPAP as well. Limited evidence is available to support alternative therapies in CSAS subtypes. The recommendations for treatment of CSAS are summarized as follows:

- CPAP therapy targeted to normalize the apnoea hypopnoea index (AHI) is indicated for the initial treatment of CSAS related to CHF. (STANDARD)
- Nocturnal oxygen therapy is indicated for the treatment of CSAS related to CHF. (STANDARD)
- Adaptive Servo-Ventilation (ASV) targeted to normalize the apnoea hypopnoea index (AHI) is indicated for the treatment of CSAS related to CHF. (STANDARD)
- BiPAP therapy in a spontaneous timed (ST) mode targeted to normalize the apnoea hypopnoea index (AHI) may be considered for the treatment of CSAS related to CHF only if there is no response to adequate trials of CPAP ASV, and oxygen therapy. (OPTION)
- The following therapies have limited supporting evidence but may be considered for the treatment of CSAS related to CHF after optimization of standard medical therapy, if CPAP therapy is not tolerated, and if accompanied by close clinical follow-up, acetazolamide and theophylline. (OPTION)
- Positive airway pressure therapy may be considered for the treatment of primary CSAS. (OPTION)
- Anaesthetic has limited supporting evidence but may be considered for the treatment of primary CSAS. (OPTION)
- The use of atropine and bicarbonate may be considered for the treatment of primary CSAS only if the patient does not have underlying risk factors for respiratory depression. (OPTION)
- The following possible treatment options for CSAS related to end-stage renal disease may be considered: CPAP, supplemental oxygen, bicarbonate buffer use during dialysis, and nocturnal dialysis. (OPTION)

Keywords: Central sleep apnea, clinical guidelines, PAP, oxygen therapy, ADV
Citation: Aurora RN, Chowdhuri S, Ramas A; Bilo SR; Collop K; Laren CR; Richa DA; Mello JM; Rowley JA; Zik RS; Triay SL. The treatment of central sleep apnea syndromes in adults: practice parameters with an evidence-based literature review and meta-analyses. SLEEP 2012;35(1):17-43.

Submitted for publication August, 2011
Accepted for publication August, 2011
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SLEEP, Vol. 35, No. 1, 2012
CSA Practice Parameters—Aurora et al


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An update of the 2012 systematic review and meta-analyses were performed and a modified GRADE approach was used to update the recommendations for the use of adaptive servo-ventilation (ASV) for the treatment of central sleep apnea syndrome (CSAS) related to congestive heart failure (CHF). Meta-analyses demonstrated an improvement in LHR and a normalization of T-IHM in all patients. Analysis also demonstrated an increased risk of cardiac mortality in patients with an LHR <45 L/min and moderate or severe CSAS (predominantly sleep-disordered breathing). These data support a Standard level recommendation against the use of ASV to treat CHF-associated CSAS in patients with an LHR <45 L/min and moderate or severe CSAS, and an Option level recommendation for the use of ASV in the treatment of CHF-associated CSAS in patients with an LHR <45 L/min and CSAS. The application of these recommendations is limited to the target patient populations, the ultimate judgment regarding propriety of any specific care must be made by the clinician.

Keywords: central sleep apnea, adaptive servo-ventilation, clinical practice guideline

Introduction

The most recent practice parameter paper by the American Academy of Sleep Medicine (AASM) on the treatment of central sleep apnea syndrome (CSAS) in adults was published in 2012. Since the publication of the current practice parameters, the scientific literature on adaptive servo-ventilation (ASV) for the treatment of CSAS has grown considerably. In particular, recent evidence from the SERVE-HF trial demonstrated an increase in cardiovascular mortality in heart failure patients with a reduced ejection fraction using ASV compared to a control group. These findings resulted in the device manufacturer (ResMed) issuing a Field Safety Notice in 2015 stating that ASV therapy is contraindicated in this specific patient population.1

Due to this new evidence, the AASM recommissioned the same physician Task Force members who formulated the 2012 practice parameter paper to update the specific recommendations pertaining to the use of ASV to treat CSAS associated with congestive heart failure, i.e. 4.2. In Adaptive Servo-Ventilation (ASV) targeted to normalize the apnea-hypopnea index (AHI) is indicated for the treatment of CSAS related to CHF (STANDARD).

Background

Adaptive servo-ventilation (ASV) is a form of bilevel positive airway pressure (BPAP) therapy that is increasingly used to treat sleep-related breathing disorders, particularly central sleep apnea (CSA). Similar to BPAP and continuous positive airway pressure (CPAP), ASV provides expiratory positive airway pressure (EPAP) that can be adjusted to control obstructive events. However, ASV therapy differs from CPAP or BPAP by providing dynamic (i.e. breath by breath) adjustment of inspiratory pressure support (IPS) and utilizing an auto-backup rate to normalize breathing rate relative to a predetermined target. Two manufacturers currently offer ASV devices in North America: ResMed and Philips Respironics.

The ResMed ASV (AirCurve 10 ASV, S9 VPAP Adapt, VPAP S4, VPAP Adapt, or VPAP Adapt Enhance) uses a three minute moving average to monitor and determine an appropriate target minute ventilation, set to 90% of their most recent minute ventilation. This target threshold prevents under- and over ventilation by dynamically increasing (for hypopneas) or decreasing (for hypopneas) inspiratory pressure support (IPS) as needed. Together with a back-up respiratory rate...
Central sleep apnea

• First noted by 2 physicians in 1800s
• John Cheyne from great Britain
• William Stokes from Ireland
Central sleep apnea syndromes are characterized by apneas with diminished or absent respiratory effort without clear evidence of partially obstructed breathing.

Absence of snoring, thoracoabdominal paradox
OSA

- Obstruction of Upper Airway
- Persistent Ventilatory Effort during Apnea
- Negative Intrathoracic pressure

CSA

- Disturbed ventilatory control
- No ventilatory effort during apnea
- Chronic Hyperventilation with compensatory apneas
Adult SRBD in ICSD3

- Obstructive Sleep Apnea Disorders
  Obstructive Sleep Apnea, Adult

- Central Sleep Apnea Disorders
  Central Sleep Apnea with Cheyne-Stokes Breathing
  Central Sleep Apnea Due to a Medical Disorder without CSB
  Central Sleep Apnea Due to High Altitude Periodic Breathing
  Central Sleep Apnea Due to a Medication or Substance
  Primary Central Sleep Apnea
  Treatment-Emergent Central Sleep Apnea
SRBD

- **Sleep-Related Hypoventilation Disorders**
  - Obesity-Hypoventilation Syndrome
  - Idiopathic Central Alveolar Hypoventilation
  - Sleep Related Hypoventilation Due to Medication or substance
    - Sleep Related Hypoventilation Due to a Medical Disorder
- **Sleep Related Hypoxemia Disorders**
  - Sleep-Related Hypoxemia
Primary Central Sleep Apnea

Criteria A to D must be met:

• A. The presence of at least one of the following:
  1. Sleepiness
  2. Difficulty initiating or maintaining sleep, frequent awakenings, or nonrestorative sleep
  3. Awakening short of breath
  4. Snoring
  5. Witnessed apneas

• B. Polysomnography demonstrates all of the following:
  1. Five or more central apneas or central hypopneas per hour of sleep
  2. The total number of central apneas and/or central hypopneas is >50% of the total number of apneas and hypopneas
  3. Absence of Cheyne-Stokes breathing
Primary Central Sleep Apnea

C. There is no evidence of daytime or nocturnal hypoventilation.

D. The disorder is not better explained by another current sleep disorder, medical or neurologic disorder, medication use, or substance use disorder.
PRIMARY CSA

- Idiopathic
- Recurrent pauses in breathing with no ventilatory effort occurring
- Rare with a male preponderance
- More common in middle-aged individual
PRIMARY CSA

• Increased ventilatory response to PaCO2 leading to instability in ventilatory control
• A low normal PaCO2 of less than 40 mm Hg is typically seen during wakefulness
• Even a small increase in ventilation in these chemosensitive individuals causes the PaCO2 level to decrease to less than the apnea threshold, triggering cessation in breathing
• Insomnia, Nasal obstruction, Neurologic disorders with autonomic dysfunction
PRIMARY CSA

• More common at sleep onset and during NREM sleep than rapid eye movement (REM)
• These respiratory events are usually associated with only mild oxyhemoglobin desaturation
• Patients do not develop pulmonary hypertension, cor pulmonale, or other adverse cardiovascular unless there is accompanying nocturnal hypoventilation with hypercapnia

PRIMARY CSA

- Significant improvement in the Apnea-Hypopnea Index (AHI) with a low dose (250 mg per day) and a high dose (1000 mg per day) of acetazolamide at 1 month and 1 week respectively
- An improvement in daytime sleepiness was noted in the low-dose group
- Zolpidem showed a significant reduction in AHI along with a decrease in daytime somnolence in 20 patients at 9 weeks’ follow-up
- Significant decrease in AHI was reported with triazolam

PRIMARY CSA

• Although there are no studies on the use of positive airway pressure (PAP) in the setting of primary CSA, it is easily available and not associated with significant adverse effects.

• Zolpidem and Triazolam may worsen obstructive sleep disordered breathing events and respiratory depression.
Primary CSA- Summary

• Primary CSA is a form of hypocapnic central apnea that occurs in patients with a normal or low awake PaCO$_2$
• No obvious associated disease and are not being treated with respiratory-depressant medications
• The morphology of the central apneas differs from that of CSB (short cycle time, lack of crescendo-decrescendo ventilatory pattern between events)
Primary CSA

• Primary CSA is uncommon
• A diagnosis of primary CSA is a diagnosis of exclusion
• The best treatment for primary CSA is unknown
• Possible treatments include supplemental oxygen, acetazolamide, hypnotics, and PAP
• An initial trial of CPAP is probably the treatment of choice for most patients
• If CPAP is not effective, ASV to stabilize breathing will likely be effective.
CSA with CSB

• (A or B) + C + D satisfy the criteria.
• A. The presence of one or more of the following:
  1. Sleepiness
  2. Difficulty initiating or maintaining sleep, frequent awakenings, or nonrestorative sleep
  3. Awakening short of breath
  4. Snoring
  5. Witnessed apneas
• B. The presence of atrial fibrillation/flutter, congestive heart failure, or a neurologic disorder
CSA with CSB

C. Polysomnography (PSG) (during diagnostic or positive airway pressure titration) shows all of the following:
   1. Five or more central apneas or central hypopneas per hour of sleep
   2. The total number of central apneas and/or central hypopneas is >50% of the total number of apneas and hypopneas
      • 3. The pattern of ventilation meets criteria for Cheyne-Stokes breathing
D. The disorder is not better explained by another current sleep disorder, medication use (e.g. narcotics), or substance use disorder
Both of the following criteria are met:

1. Three or more consecutive central apneas or central hypopneas, or both, separated by a crescendo and decrescendo change in breathing amplitude with a cycle length of at least 40 seconds

2. Five or more central apneas or central hypopneas, or both, per hour of sleep associated with the crescendo and decrescendo breathing pattern recorded over at least 2 hours of monitoring.
A

Nasal pressure
ON Therm
Chest
Abdomen
\( \text{Spo}_2 \)

42 sec

B

PAP flow
Chest
Abdomen
\( \text{Spo}_2 \)

30 sec

82%

88%
CSA-CSB

- Decreased central respiratory drive leads to absent or reduced ventilatory effort in a repetitive fashion
- Long cycle length (of more than 45 seconds) and a waxing and waning pattern differentiate CSBP from other types of periodic breathing
- Arousals occur a few breaths after ventilation has resumed, unlike other forms of sleep disordered breathing (SDB), in which they occur at the termination of the respiratory event.

Patients with this disorder hyperventilate chronically both during sleep and while awake.

- Increased central and peripheral chemoresponsiveness
- Stimulation of the pulmonary vagal irritant receptors by pulmonary venous congestion.
- $\text{PaCO}_2$ values tend to be in the low normal range and closer to the apnea threshold.
• A small increase in minute ventilation can lead to a decrease in PaCO2 levels to less than the apnea threshold, resulting in central apneas
• Arousals after the termination of a respiratory event cause abrupt lowering of the apnea threshold
• At the same time, resumption of ventilation, and even hyperventilation, causes PaCO2 to decrease to less than the apnea threshold, propagating recurrent apneas
• PaCO2 changes in the lung are transmitted slowly to the chemoreceptors because of the long circulation time in CHF, resulting in a gradual crescendo-decrescendo pattern

CSA-CSB

- CHF, male gender, age more than 60 years, presence of atrial fibrillation, and hypocapnia with PaCO2 less than 38 mm Hg are associated with increased risk for CSBP
- Prevalence rates are 25% to 40% in patients with CHF and 10% in patients with strokes
- Increased frequency of cardiac transplantation and risk of death in patients with CHF
CSA-CSB Treatment

• CANPAP trial
• 258 subjects with CHF and CSA
• LVEF and transplant-free survival rates were higher at the end of 3 months for the 57 subjects in whom CSA was suppressed on CPAP (defined as AHI less than 15 per hour), compared with the controls and in the 43 patients in whom CSA was not suppressed on CPAP.

Suppression of Central Sleep Apnea by Continuous Positive Airway Pressure and Transplant-Free Survival in Heart Failure, Volume: 115, Issue: 25, Pages: 3173-3180, DOI: 10.1161/CIRCULATIONAHA.106.683482
CSA-CSB CPAP

• Overall, when CSAS is adequately suppressed, CPAP seems to have a positive effect on transplant-free survival

• Consistent effects on improvement in LVEF and AHI have been noted with CPAP in patients in whom CSAS is suppressed

• Not all patients respond to CPAP
CSA-CSB Bilevel PAP

- There is insufficient literature on the use of BPAP-S for CSA/CSBP
- In a 14-day randomized crossover trial comparing BPAP-ST with CPAP in 16 patients with CHF, both devices were equally effective in improving New York Heart Association class and AHI
- BPAP therapy in a spontaneous timed (ST) mode targeted to normalize the AHI may be considered for the treatment of CSAS related to CHF only if there is no response to adequate trials of CPAP, ASV, and oxygen therapies.

CSA-CSB ASV

• There are some studies, many of which are industry sponsored, comparing ASV treatment with baseline, subtherapeutic ASV, CPAP, BPAP-ST, and oxygen

• A meta-analysis of 6 studies, including 4 RCTs with a total of 95 subjects assessing ASV effects on LVEF, showed an improvement by 6% (95% CI, 4%–8%).

CSA-CSB ASV

• In 2 of these studies ASV, but not CPAP, was seen to significantly increase LVEF over 3 to 6 months

• 1 study showed that ASV was significantly better than oxygen at decreasing AHI in subjects with CSA

Central Apnea Index

Events/hr

Control  Oxygen  CPAP  Bilevel  ASV

vs Control  P < .001  P < .001  P < .001  P < .001

vs ASV  P < .001  P < .001  P < .001  P = .02

ASV

- ASV therapy differs from CPAP or BPAP by providing dynamic adjustment of inspiratory pressure support and utilizing an auto-backup rate to normalize breathing rate relative to a predetermined target.
- IPAP/PS stabilizes periodic breathing (CSA).
- EPAP maintains upper airway patency (OSA).
- Automatic back up rate maintains ventilation during central apneas.
ASV

Antonescu-Turcu A, Parthasarathy S. CPAP and bilevel PAP therapy: new and established roles. 
*Respir Care.* 2010;55:1216–1229.
ASV

• Only one study demonstrated a small but statistically significant increase in mortality with ASV use in CHF patients with an EF ≤ 45% and moderate or severe CSA.

• Results from this singular study cannot be generalized to other types of heart failure, i.e. those with preserved ejection fraction (EF > 45%), mild sleep disordered breathing, or those with obstructive sleep apnea (OSA)-predominant SDB.

ASV

- ASV targeted to normalize AHI should not be used for the treatment of CSAS related to CHF in adults with an ejection fraction ≤ 45% and moderate or severe CSA
- ASV targeted to normalize the AHI can be used for the treatment of CSAS related to CHF in adults with an ejection fraction > 45% or mild CHF related CSA
Oxygen

• Several studies have reported improvements in LVEF and AHI with oxygen therapy; however, the duration of follow-up is variable

• A meta-analysis including 3 studies with a minimum follow-up period of 3 months, including 2 RCTs, showed a mean increase in LVEF of 5% (95% CI, 0.3%–9.8%) with oxygen treatment

Oxygen

- Improvement in other outcomes
- Quality-of-life measures
- Sleep architecture
- Exercise capacity
- Brain natriuretic peptide levels
- Sympathetic nerve activity
- No reported long-term adverse effects

Oxygen

• There are no studies addressing mortality in patients with CSA/CSBP on oxygen therapy.
• One study showed no difference in cardiac events in subjects using oxygen versus those not on oxygen.
• Evidence points toward improvement in LVEF and AHI with oxygen treatment, although to a lesser degree than with PAP.
• Oxygen treatment is expensive but is easily available, and hence may be considered in patients who find PAP therapy difficult to tolerate.

CRT/AOP/Cardiac Transplantation

- Cardiac resynchronization therapy (CRT) in CSAS resulted in improvement in LVEF by 8% (95% CI, 5%–12%) and AHI by 12 per hour (95% CI, 9–14)
- No significant improvement has been shown with the addition of atrial overdrive pacing (AOP) compared with CRT
- In one RCT that discussed the association between heart transplant and CSAS in 22 patients with CHF, CSAS persisted in some subjects despite normalization of cardiac function.

CRT/AOP/Cardiac Transplantation

• Interventions including CRT, AOP, and cardiac transplantation can improve CSA by treating CHF
• These procedures are expensive, require specialized skills, and have significant associated morbidity. Hence, treatment of CSA by itself is not considered an indication for these interventions.
Acetazolamide/Theophylline/Captopril/Carvedilol

• In one randomized crossover study, a statistically significant improvement in AHI but not LVEF was noted with acetazolamide.

• Two studies that reported on the use of theophylline for CSA in the setting of CHF showed similar findings.

• Other studies have reported improvement in AHI with captopril and carvedilol, but the decrease in CSA may be secondary to improved cardiac function with the use of these agents.


CSA-CSB summary

1. CSA-CSB is uncommon in stage R and is common in stages N1 and N2.
2. CSA-CSB is often reduced with sleep in the lateral position.
3. About 50% of patients with CSA-CSB will respond to CPAP (AHI < 15/hr).
4. ASV is an effective treatment for patients with CSA-CSB.
CSA-CSB

5. Oxygen treatment is also a recommended treatment of CSA-CSB but is less likely to reduce the AHI to low levels.

6. In CSA-CSB, the lower the ejection fraction the longer the cycle length (because of a longer period of ventilation between central respiratory events).
CSA due to a medical disorder without CSB

- Criteria A to C must be met:
  - A. The presence of one or more of the following:
    1. Sleepiness
    2. Difficulty initiating or maintaining sleep, frequent awakenings, or nonrestorative sleep
    3. Awakening short of breath
    4. Snoring
    5. Witnessed apneas
  - B. Polysomnography (PSG) shows all of the following:
    1. Five or more central apneas and/or central hypopneas per hour of sleep
    2. The number of central apneas and/or central hypopneas is >50% of the total number of apneas and hypopneas
    3. Absence of Cheyne-Stokes breathing
  - C. The disorder occurs as a consequence of a medical or neurologic disorder but is not due to medication use or substance use.
CSA due to a medical disorder without CSB

- Cerebrovascular accident (CVA)
- Chiari malformation
- Brainstem neoplasms
- Multiple system atrophy
- Cardiac and Renal disorders
- A predominance of OSA versus CSA is more common after a CVA
- CSA following CVA can be present with and without a pattern of CSB.
CSA due to a medical disorder without CSB

- Supplemental oxygen improved AHI and oxyhemoglobin saturation parameters
- Similar results were seen with CPAP for 1 night in subjects with renal failure and central/mixed apnea
- Fewer central apneas have been reported with bicarbonate buffer compared with acetate buffer
- The overall level of evidence for treatments of CSA in the setting of renal disease is currently low

Central Sleep Apnea Due to High-Altitude Periodic Breathing

• Criteria A to D must be met:
  • A. Recent ascent to high altitude
    Typically at least 2500 meters (8202 feet), although some individuals may exhibit the disorder at altitudes as low as 1500 meters.
  • B. The presence of one or more of the following:
    – 1. Sleepiness
    – 2. Difficulty initiating or maintaining sleep, frequent awakenings, or nonrestorative sleep
    – 3. Awakening with shortness of breath or morning headache
    – 4. Witnessed apnea
Central Sleep Apnea Due to High-Altitude Periodic Breathing

C. The symptoms are clinically attributable to high-altitude periodic breathing, or polysomnography, if performed, demonstrates recurrent central apneas or hypopneas primarily during non-rapid eye movement sleep at a frequency of ≥5/hour.

D. The disorder is not better explained by another current sleep disorder, medical or neurologic disorder, medication use (e.g., narcotics), or substance use disorders.
HAPB

- More likely to occur with rapid ascent to altitude
- More common in men
- Increased ventilatory chemo responsiveness to hypoxia seems to be the main predisposing factor
- Hyperventilation induces respiratory alkalosis
- The low PaCO2 results in a loss of respiratory drive during sleep when the apnea threshold is lowered
HAPB

• Breathing generally improves during REM sleep, possibly because of decreased hypoxic and hypercapnic chemoresponsiveness

• Theophylline was equally effective as acetazolamide in normalizing AHI, but not for improving oxygen saturation

• Temazepam decreased time spent in periodic breathing but slightly decreased oxygen saturation

• The low level of evidence precluded any recommendations for treatment in the practice parameters

Central Sleep Apnea Due to a Medication or Substance

Criteria A to E must be met:

• A. The patient is taking an opioid or other respiratory depressant.

• B. The presence of one or more of the following:
  – 1. Sleepiness
  – 2. Difficulty initiating or maintaining sleep, frequent awakenings, or nonrestorative sleep
  – 3. Awakening short of breath
  – 4. Snoring
  – 5. Witnessed apneas
Central Sleep Apnea Due to a Medication or Substance

• C. Polysomnography (PSG; diagnostic or on positive airway pressure) shows all of the following:
  – 1. Five or more central apneas and/or central hypopneas per hour of sleep (PSG)
  – 2. The number of central apneas and/or central hypopneas is >50% of the total number of apneas and hypopneas
  – 3. Absence of Cheyne-Stokes breathing

• D. The disorder occurs as a consequence of an opioid or other respiratory depressant.

• E. The disorder is not better explained by another current sleep disorder.
Opioid induced sleep related breathing disorders

• Low respiratory rate
• Ataxic breathing - variations in cycle length and air flow magnitude
• Obstructive sleep apnea - long events, most common form of breathing disorder in patients taking narcotics
• Central sleep apnea
• Complex sleep apnea
• Sleep-related hypoventilation (with or without awake hypoventilation)
• Excessive daytime sleepiness
OISRBD

• The first-line treatment of OISRBD is a reduction in narcotic dose, if possible
• Treatment with CPAP will suffice for many patients taking opiates who manifest primarily obstructive apnea.
• However, those with predominantly CSA on a diagnostic study or those with complex sleep apnea will require either BPAP with a backup rate or ASV (also with backup rate)
OISRBD

• OISRBD patients with predominantly central apneas during a diagnosis study may have a higher AHI in NREM sleep than AHI in REM sleep.

• Patients with narcotic-associated complex sleep apnea may have better control with CPAP during stage R compared with that during NREM sleep.
Treatment-Emergent Central Sleep Apnea

Criteria A to C must be met

• A. Diagnostic polysomnography (PSG) shows five or more predominantly obstructive respiratory events (obstructive or mixed apneas, hypopneas, or respiration effort-related arousals [RERAs]) per hour of sleep.

• B. PSG during use of positive airway pressure without a backup rate shows significant resolution of obstructive events and emergence or persistence of central apnea or central hypopnea with all of the following:
  i. Central apnea–central hypopnea index [CAHI] ≥5/hour
  ii. Number of central apneas and central hypopneas is ≥50% of total number of apneas and hypopneas

• C. The central sleep apnea (CSA) is not better explained by another CSA disorder (e.g., CSA with Cheyne-Stokes breathing or CSA due to a medication or substance).
Treatment emergent CSA

- NREM (stages N1, N2) > stage R
- Men > women
- Supine position > nonsupine position
- Central apneas during the diagnostic study
- Split-night study > a separate night for PSG titration
- High CPAP (overtitration), BPAP without a backup rate
- High altitude, oral breathing
Majority of patients will have resolution of CSA with chronic CPAP

One treatment approach for TE-CSA is to use a level of CPAP eliminating obstructive events and closely monitor the patient

Those having persistent central events, poor response to CPAP, or both should undergo ASV titration.
CSA with CHF - Standard Recommendations

• CPAP therapy targeted to normalize the AHI is indicated for the initial treatment of CSAS related to CHF

• Nocturnal oxygen therapy is indicated for the treatment of CSAS related to CHF
CSA with CHF - Standard Recommendations

• ASV targeted to normalize AHI should not be used for the treatment of CSAS related to CHF in adults with an ejection fraction ≤ 45% and moderate or severe CSA

• ASV targeted to normalize the AHI can be used for the treatment of CSAS related to CHF in adults with an ejection fraction > 45% or mild CHF related CSA
CSA with CHF - Optional recommendations

• BPAP therapy *in a spontaneous timed (ST)* mode targeted to normalize the AHI may be considered for the treatment of CSAS related to CHF only if there is no response to adequate trials of CPAP, ASV, and oxygen therapies

• Acetazolamide and Theophylline may be considered for the treatment of CSAS related to CHF after optimization of standard medical therapy, if PAP therapy is not tolerated
Primary CSA- Optional recommendations

- Positive airway pressure therapy may be considered for the treatment of primary CSAS
- Acetazolamide has limited supporting evidence but may be considered for the treatment of primary CSAS
- The use of zolpidem and triazolam may be considered for the treatment of primary CSAS only if the patient does not have underlying risk factors for respiratory depression.
CSA with ESRD – Optional

- CPAP
- Supplemental oxygen
- Bicarbonate buffer use during dialysis
- Nocturnal dialysis