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Obstructive Sleep Apnea

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Executive Summary

- Obstructive sleep apnea (OSA) includes symptoms of excessive daytime somnolence, snoring, and witnessed apneic events.
- The average number of hypopneic and apneic events per hour of sleep are used to grade the severity of OSA using the apnea-hypopnea index.
- The gold standard for diagnosing OSA is through full-night polysomnography in a laboratory with a titration to determine the optimal pressure setting.

- Split-night diagnostic titration studies using auto-titration devices are not the diagnostic study of choice.
- Continuous positive airway pressure (CPAP) devices remain the mainstay of treatment. If CPAP is poorly tolerated, alternatives include Bi-level PAP, oral devices, and surgical options.
- Emerging therapies, such as hypoglossal nerve stimulation, are being developed. These alternatives to CPAP are being studied in efforts to improve patient adherence and outcomes associated with OSA.

Definition

In 2009, the Adult Obstructive Sleep Apnea Task Force of the American Academy of Sleep Medicine (AASM) defined obstructive sleep apnea (OSA) as “the occurrence of daytime sleepiness, loud snoring, witnessed breathing interruptions, or awakening due to gasping or choking in the presence of at least six obstructive respiratory events (apneas, hypopneas, or respiratory effort related arousals per hour of sleep). The presence of 15 or more obstructive respiratory events per hour of sleep in the absence of sleep-related symptoms is also sufficient for the diagnosis of OSA”.¹ The symptoms of OSA are summarized in Table 1.

AASM defines hypopneas as a “reduction in airflow,” while an obstructive apnea is a “complete cessation of airflow despite ongoing inspiratory efforts.”² This can lead to a reduction in oxyhemoglobin saturation and arousal from sleep. The apnea-hypopnea index (AHI) is used to assess the severity of sleep apnea.

Epidemiology

OSA is the most common sleep-related disorder.³ Although the exact prevalence is unknown, estimates range from 10-17% in the United States.⁴ Improvements in diagnostic technology and more clearly defined diagnostic criteria appear to point to higher prevalence of OSA than previously believed, as high 23.4% in women and 49.7% in men.⁵ Diseases that increase risk for OSA include: obesity, atrial fibrillation, cardiovascular disease, cerebrovascular disease, congestive heart failure, Type 2

diabetes mellitus (T2DM), pulmonary hypertension, and resistant hypertension.^{1,6} Severe untreated OSA has been associated with increased all-cause mortality.^{3,4}

Race

A racial disparity exists in OSA. African Americans appear to develop sleep-disordered breathing approximately 8 years earlier than Caucasians, and patients younger than 25 years of age had higher numbers of apneic events.⁷ OSA rates in Asia appear to be similar to that of the United States, despite lower body mass index (BMI). Craniofacial and soft tissue differences in the upper airway increase the chance of OSA and are thought to explain why Asians have similar rates of OSA.^{1,8}

Obesity

Obstructive sleep apnea is twice as prevalent in obese compared to normal weight individuals.⁹ According to the United States National Health and Nutrition Examination Survey database, estimated prevalence of OSA increased by as much as 50% between 1990 and 2010 in every age and BMI category studied.¹⁰ Growing rates of obesity will continue to contribute to an increasing OSA prevalence.¹¹ Over a 4-year period, the Wisconsin Sleep Cohort Study demonstrated worsening AHI with higher levels of obesity.³

Gender

Men are two to three times more likely to have OSA.¹² The mechanism for why this disparity exists is poorly understood. This difference in risk is independent of age and BMI.⁸ However, during menopause, the prevalence of OSA in women is closer to that of men.¹²

Age

Young adulthood through the seventh decade is most affected by OSA.^{3,13} Rates increase with age, particularly in adults older than 60 years.⁴ Age-related reasons for increased OSA rates include changes in the pharyngeal bony and soft-palate structures

and increased adiposity.⁶ In pediatric patients, high-risk groups for sleep apnea include the obese, those with adenoid and tonsillar hypertrophy, craniofacial abnormalities, Down syndrome, and neuromuscular disorders.^{16,17} The overall prevalence in children is 1-5%.¹⁸

Other Risk Factors

Although less evidence exists, some observational studies report higher levels of OSA in smokers and those with chronic rhinitis, congestive heart failure, chronic obstructive pulmonary disease, cerebrovascular accidents, end-stage renal disease, and hypothyroidism.⁶

Public Health Impact

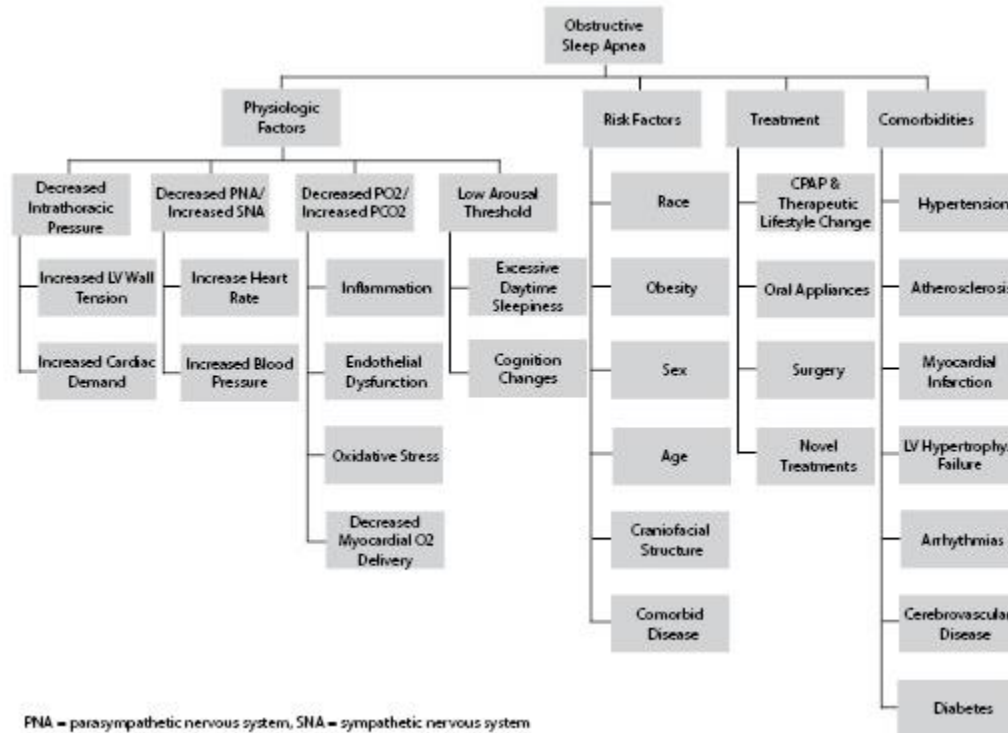
The exact cost of OSA is unknown. In 2002, estimates of \$132 billion were spent on OSA.²⁰ Of the \$132 billion, an estimated \$15.9 billion was spent on the 800,000 crashes attributed to OSA.²⁰ Noncommercial drivers having motor vehicle crashes are more likely to have OSA.¹³ A recent study of 1478 patients with OSA estimated an increased motor vehicle risk ratio of 2.45 among patients compared with control ($P < 0.001$).²¹ Treatment of OSA with CPAP does improve the driver's performance and reduce the incidence of motor vehicle crashes.^{21,22}

Pathophysiology

The pathophysiology of OSA, once thought to simply be due to recurrent obstruction in the upper airway resulting in apnea or hypopnea, is now thought to be more complex and variable than this original theory.¹ In most patients, multiple underlying factors lead to development of OSA. Some common examples include anatomical compromise in the pharyngeal airway, craniofacial anatomical features, dilator muscle weakness and/or dysfunction, supine/positional sleep apnea, unstable ventilatory control leading to imbalances in carbon dioxide and oxygen pressure levels, and lower thresholds for arousal from sleep.^{4,23} This cascade of events, alone or in combination, leads to physiologic changes in the body that result in the late cardiovascular, cerebrovascular, and psychological changes associated with untreated apnea.²⁴ Figure 1 demonstrates the pathophysiology consequences of OSA.

Figure 1. Physiologic Factors, Risk Factors, Treatment, and Comorbidities of OSA

PNA = parasympathetic nervous system, SNA = sympathetic nervous system



Screening for Obstructive Sleep Apnea

The United States Preventive Services Task Force (USPSTF) is expected to make a recommendation for routine screening of OSA by 2016.²⁵ Currently, the USPSTF does not have a recommendation for routine OSA screening.²⁵ Concordantly, the AASM does not recommend universal screening for sleep apnea.¹ Targeted diagnostic polysomnography (PSG) should occur if symptoms exist (see Table 1) or if risk factors, including obesity, craniofacial, or upper airway abnormalities, are present.^{1,11}

Table 1. Symptoms of Obstructive Sleep Apnea

- Daytime somnolence
- Difficulty concentrating or memory loss
- Fatigue
- Insomnia
- Mood changes
- Morning headaches
- Non-restorative sleep

Table 1. Symptoms of Obstructive Sleep Apnea

Snoring
Vivid dreams
Witnessed apnea
Awakening due to gasping or choking

There are multiple screening tools available. These scales are often utilized as a prescreen to help determine if a patient should undergo further testing. The Epworth Sleepiness Scale (ESS) is the most commonly used questionnaire to prescreen patients for OSA.⁴ As depicted in Table 2, ESS is self-administered and allows patients to rate their likelihood of falling asleep in eight daily activities.^{26,27} All questions must be answered for ESS to be a validated prescreen. A meta-analysis by the American College of Physicians determined this questionnaire had a low accuracy for diagnosis of OSA but that it does correlate with severity of OSA.⁴ A follow-up study by the ESS author determined a cutoff of > 10 is considered excessively sleepy.²⁸

Table 2. Epworth Sleepiness Scale (ESS)

Use the following scale to choose the most appropriate number for each situation:

- 0 = would never doze
- 1 = slight chance of dozing
- 2 = moderate chance of dozing
- 3 = high chance of dozing

It is important that you answer each question as best you can:

Situation	Chance of Dozing			
Watching TV	0	1	2	3
Sitting, inactive in a public place (e.g., a theater or meeting)	0	1	2	3
Sitting as a passenger in a car for an hour without a break	0	1	2	3
Lying down to rest in the afternoon when circumstances permit	0	1	2	3
Sitting and talking to someone	0	1	2	3
Sitting quietly after a lunch without alcohol	0	1	2	3
Sitting in a car, while stopped for a few minutes in the traffic	0	1	2	3

Table 2. Epworth Sleepiness Scale (ESS)

Use the following scale to choose the most appropriate number for each situation:

0 = would never doze

1 = slight chance of dozing

2 = moderate chance of dozing

3 = high chance of dozing

It is important that you answer each question as best you can:

Situation

Chance of Dozing

Scores of 0-9 indicate low possibility of OSA.

Scores of 10-24 should seek expert care.

Scores of 16 and greater indicate possibility of severe OSA or narcolepsy

Adapted from: Johns MW. A new method for measuring daytime sleepiness: The Epworth sleepiness scale. *Sleep* 1991;14:540-545.

Sitting and reading

0 1 2 3

The same meta-analysis by the American College of Physicians demonstrated the Berlin Questionnaire, as depicted in Table 3, may be helpful in predicting risk for OSA.⁴The questionnaire had a wide range in sensitivity and specificity depending on the AHI cutoff level. Since no clinical model can predict severity of OSA,^{1,19} PSG remains the gold-standard for diagnosis of OSA.¹ The Berlin Questionnaire and ESS have been used in multiple randomized, controlled studies, despite the lack of evidence.⁴ These questionnaires also have been used to monitor symptoms after initiating therapies for those diagnosed with OSA. These questionnaires are helpful to initiate discussions with at-risk patients.

Table 3. Berlin Questionnaire

Category 2

6. How often do you feel tired or fatigued after your sleep?

a. Nearly every day

b. 3-4 times a week

Table 3. Berlin Questionnaire

c. 1-2 times a week

d. 1-2 times a month

e. never or nearly never

7. During your wake time, do you feel tired, fatigued, or not up to par?

a. Nearly every day

b. 3-4 times a week

c. 1-2 times a week

d. 1-2 times a month

e. never or nearly never

8. Have you ever nodded off or fallen asleep while driving a vehicle?

a. Yes b. No

Category 3

9. Do you have high blood pressure?

a. Yes b. No c. Don't know

10. BMI > 30 kg/m²?

a. Yes b. no

To score, add points from each category.

- Category 2 is positive if the total score is 2 or more points.

- Category 3 is positive if the answer to item 9 is Yes OR if the BMI is > 30 kg/m².

High Risk for OSA: if there are 2 or more categories where the score is positive

Low Risk for OSA : if there is 1 or no categories where the score is positive

Category 1

1. Do you snore?

a. Yes b. No c. Don't Know

Table 3. Berlin Questionnaire

If you snore

2. Your snoring is?

a. Slightly louder than breathing

b. As loud as talking

c. Louder than talking.

d. Very loud. Can be heard in adjacent rooms.

3. How often do you snore?

a. Nearly every day

b. 3-4 times per week

c. 1-2 times per week

d. 1-2 times a month

e. never or nearly never

4. Has your snoring ever bothered other people?

a. Yes b. No

5. Has anyone noticed that you quit breathing during your sleep?

a. Nearly every day

b. 3-4 times a week

c. 1-2 times a week

d. 1-2 times a month

e. never or nearly never

Diagnosis of OSA

A thorough history and physical exam to evaluate for OSA should occur if a patient exhibits risk factors or symptomatology suggestive of sleep apnea. Common presenting complaints of OSA include snoring and daytime somnolence. In a systematic review of the accuracy of clinical examination in the diagnosis of OSA, the most useful individual findings for identifying patients with OSA was nocturnal choking or gasping.

Snoring was less specific for identifying patients with OSA.²⁹ Physical exam should include anthropometrics, such as neck circumference and BMI. A neck circumference > 17 inches in men and > 16 inches in women warrants further investigation for OSA.¹ A BMI > 30 kg/m², which is diagnostic for obesity, is also an independent risk factor for OSA.¹ The physical exam should include an evaluation of the mouth for uvula enlargement, tonsillar hypertrophy, and high arched/narrow hard palate, and the nose for polyps, septal deviation, and turbinate hypertrophy.

The Mallampati score, a grading system of crowding in the oropharynx used by anesthesiologists to identify patients at risk for difficult intubation, was shown to be useful in evaluating patients at risk for OSA independent of other physical risk factors.³⁰ Patients are graded on a scale of I-IV based on visualization of the uvula and soft palate with the mouth open and tongue protruded (*see Figure 2*). Patients are told to open their mouth and stick out their tongue as far as possible without emitting a sound. For every 1 point increase in the Mallampati score, the odds of having OSA increased by more than two-fold and the AHI increased by more than nine times.

Figure 2. Mallampati Airway Classification (I-IV Scale)

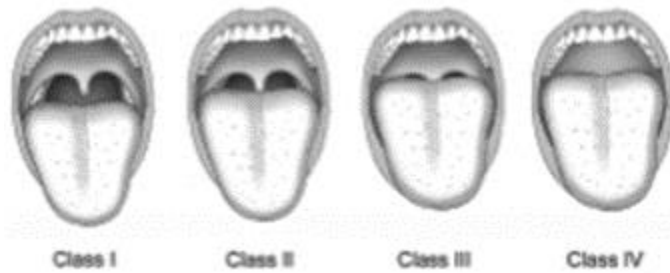
Class I: soft palate and entire uvula visible

Class II: soft palate and portion of uvula visible

Class III: soft palate visible (may include base of uvula)

Class IV: soft palate not visible

Figure 2. Mallampati Airway Classification (I-IV Scale)



PSG at a sleep laboratory and home testing with portable monitors are two options for diagnosing OSA.¹ Each testing has its limitations that will be further discussed.

Polysomnography

The AASM and the American College of Physicians recommend that PSG evaluation include “electroencephalogram, electrooculogram, chin electromyogram, airflow, oxygen saturation, respiratory effort, and electrocardiogram.”^{1,4} Furthermore, the AASM recommends testing for OSA only at an accredited sleep laboratory.¹ PSG technicians should have training through an accredited sleep technologist education program or allied health education program.¹ All PSGs should be evaluated by a board-certified sleep medicine physician. Full-night PSG should be used for diagnosis of OSA.¹ The diagnosis of OSA is confirmed and graded using the AHI.^{1,15} The AHI is defined by the “number of obstructive events (apneas, hypopneas + respiratory event-related arousals) on PSG” per hour of sleep.¹ The AASM threshold for diagnosing OSA is asymptomatic with AHI more than 15 events per hour or symptomatic (e.g., unintentional sleep episodes during daytime, daytime somnolence, fatigue, insomnia, waking up gasping or choking, confirmed snoring, breathing interruptions during sleep) with more than five events per hour. Table 4 demonstrates the AHI index with diagnosis and severity of OSA. High-quality evidence showed an association between AHI > 30 and greater with all-cause mortality.¹¹

Table 4. AHI Index, Diagnosis, and Severity of OSA

AHI index = 15 without symptoms = OSA

AHI index > 30 = severe OSA

AHI index = 5 with symptoms = OSA

Major limitations to PSG include high cost (ranging from hundreds to thousands of dollars depending on geographic location and facility fees), specialized resources, and time to complete study.¹¹ This can be difficult for patients living in geographically rural areas. Underserved patients and those with transportation difficulties may also have difficulty completing PSG.

Split-night Study

A split-night study — an initial diagnostic PSG is followed by a CPAP titration on the same night — is an alternative to PSG testing.¹ Split-night studies potentially require the patient to come to the sleep lab only once, cutting the cost of testing in half and decreasing the time burden required to diagnose and initiate treatment. However, this is not the recommended diagnostic technique because split-night studies have less time to diagnose hypopneic and apneic events and less time to perform a CPAP titration.¹⁹ This may require the patient to return to the sleep lab an additional time to perform the CPAP titration.¹⁹

Testing with Portable Monitors

The AASM recommends portable monitors (PMs) should only be used in conjunction with a comprehensive sleep evaluation.¹ The AASM recommends PMs should “record airflow, respiratory effort, and blood oxygenation.” Portable monitors are at-home testing devices and best for diagnosing OSA in patients with no comorbid sleep disorders or major medical problems.^{1,4,14} The American College of Physicians recommends PMs only for patients without serious comorbidities as an alternative to PSG when PSG is not available for diagnostic testing.⁴ Patients with a high likelihood of OSA and poor sleep quality and insomnia should undergo PSG.¹⁴

When analyzing a PM test, the AHI for PMs is different than PSG. AHI for PMs is defined by AASM as “the number of apnea + hypopneas total recording time.”¹ Since sleep duration is not recorded during home sleep testing, the total test time is used to calculate AHI and may underestimate events since the patient is likely to not have them

when awake. PMs do not record body position, making a diagnosis of supine dominant OSA more difficult.¹⁵

Overnight Pulse Oximetry

During overnight pulse oximetry, the saturation of peripheral oxygen is estimated and recorded. Currently, overnight pulse oximetry is not recommended for diagnosis of OSA.²⁵ However, emerging research demonstrates in a study of 619 patients that overnight pulse oximetry may be useful in the diagnosis of severe OSA with AHI \geq 30. The overnight pulse oximetry provided an accuracy of 90.42-90.55% with sensitivity of 89.36-89.87% and specificity of 91.08-93.05%. The sensitivity and specificity for diagnosis were lower for moderate OSA (AHI = 15).³¹ Larger studies are needed to evaluate the effectiveness of using this alternative method in OSA diagnosis.

Treatment Options

Weight loss, CPAP, and mandibular devices remain the cornerstone of therapy.¹ There are different types of positive airway pressure (PAP) devices including bi-level (commonly known by the brand name BiPAP), continuous (CPAP), and autotitrating (APAP) modes. Patient preference should be considered when determining the delivery route for PAP, including nasal, oral, or oronasal. Patients who fail to utilize one type of mask should be offered an alternative prior to discontinuing PAP. Oral appliances, surgical options, and novel therapies to treat OSA are considered second-line therapies. Any severe disability or disorder causing decreased cognitive ability (i.e., Down syndrome, psychiatric diseases, and dementia) can make treating OSA difficult and may merit utilizing second-line therapies as initial treatment.

Continuous Positive Airways Pressure

CPAP is considered the gold standard treatment for patients with moderate and severe OSA.^{15,32} CPAP treatment using a facial mask was invented in 1981.³ Prior to this treatment, options were limited to dental devices, and for the most severe cases tracheotomy.³

CPAP works by applying pressure to the pharyngeal lumen greater than the pharyngeal critical pressure. By maintaining pharyngeal patency, a decrease in hypopnea and apnea events occurs.³²

In a review article by the American College of Physicians, 22 studies compared CPAP to control, finding a reduction in AHI, improved ESS scores, and higher oxygen saturation levels.¹¹ Additionally, 24 studies compared CPAP to sham CPAP treatments, finding moderate-quality evidence supporting CPAP as a superior treatment vs sham for AHI scores and ESS scores.¹¹

Benefits of CPAP include reduction of excessive daytime sleepiness, improved cognitive function, improved quality of life, reduced blood pressure in hypertensive patients, and overall reduction of cardiovascular mortality.³² Adherence to CPAP therapy is extremely variable (46-80%).³² Many reasons cause patients to be noncompliant with their therapy, including claustrophobia, discomfort, noise irritation, and skin irritation.¹¹

Predictors of adherence include more severe OSA, higher degree of daytime sleepiness, higher socioeconomic status, higher level of patient understanding of the therapy, and the type of mask used.^{32,33} Eight studies evaluated different types of masks, with adherence showing patients were much less adherent with oronasal masks compared to nasal masks.³² Nasal masks and nasal pillows had similar adherence but patients experienced more adverse symptoms (e.g., nasal congestion, nasal dryness, nosebleeds, headaches) with nasal pillows. From an efficacy standpoint, three small trials comparing oral CPAP vs nasal CPAP found insufficient evidence that one was superior to the other.¹¹

Auto-PAP

An APAP is a PAP device that detects changes in a user's respirations and can change the amount of pressure to maintain patency of airway. APAP and BiPAP are best suited for patients intolerant to CPAP.¹ Moderate-quality evidence from 21 randomized trials demonstrated that APAP and fixed CPAP have similar adherence and treatment effects for patients with OSA.¹¹ However, APAP is more expensive and can lead to more sleep fragmentation and hemodynamic effects compared to CPAP.¹⁵

Bi-level PAP

BiPAP devices are an alternative to CPAP for patients who have discomfort related to the fixed pressure of CPAP. BiPAP offers lower pressure during exhalation compared to inhalation. Insufficient evidence exists comparing BiPAP to CPAP.¹¹ However, it is a beneficial alternative for those that cannot tolerate CPAP.

Oral Appliances

Oral appliances (OAs) can improve OSA symptoms by preventing collapsibility and maintaining the upper airway passage.³⁴ Oral appliances are a good option for patients with mild-to-moderate OSA who are resistant to using CPAP.^{1,34,35} The AASM recommends all patients undergo a dental exam prior to use of OAs.¹ This should occur 6 months after fitting and then annually.¹

For all OAs, oropharyngeal crowding and obesity were predictive factors for response to oral appliance therapy.²⁰ Multiple OAs currently available include mandibular advance devices (MAD), which cover the teeth and hold the mandible in place, and tongue stabilizing devices (TSD), which hold the tongue in a forward position.

A Cochrane review in 2008 on OAs evaluated 17 studies with 831 participants. Two studies showed OAs reduced daytime sleepiness on ESS compared to controls with an improved AHI (AHI = -10.78 events/hr; 95% confidence interval [CI] = -15.53 to -6.03).³⁶ Oral appliances were significantly less effective than CPAP at reducing AHI. In another study, OAs were compared to corrective upper airway surgery. OAs lowered symptoms and improved AHI for 12 months, while this did not remain after surgery.³⁷

Mandibular advancement devices are associated with successful treatment of OSA in small sample sizes. MAD efficacy is strongest in less obese, younger, female, mild OSA, and supine OSA patients.^{3,38} In a prospective, randomized, crossover study comparing MAD to CPAP, CPAP had better resolution of symptoms, patients preferred the MAD over CPAP, and patients reported higher levels of compliance.³⁹

Several novel OAs recently have been developed in an attempt to approve both the efficacy and adherence of treatment. A multicenter, prospective, randomized crossover

trial on patients with mild to severe OSA was performed using an oral pressure therapy vacuum that works by pulling the soft palate forward and stabilizing the tongue when applied to the oropharynx. This device allows patients to breathe normally through their nose as continuous pressure is applied to the oral cavity. The study revealed that the appliance was well-tolerated and patients used it an average of 6 hours a night. Clinically significant improvements were seen in reduction of AHI, sleep quality and continuity, and daytime sleepiness symptoms.⁴⁰

TSDs help maintain the tongue in a more forward position to allow enhanced airway opening.⁴¹ A new TSD was studied in a randomized, crossover study on a small sample of patients in a tertiary sleep clinic. Patients were treated with both a TSD and MAD, and AHI, compliance, and device preference were monitored. Despite significant improvement in AHI with both devices, there was poor compliance with the TSD and patients preferred the MAD.⁴¹

A limitation of OAs up to this point has been their inability to record objective data. Subjective data from patient reporting has been the only available data used in previous studies on OAs. A novel OA sensor device has recently been created that can be used to measure compliance. Initial research shows a high correlation between patient reporting and monitor data in regards to compliance with the OA.⁴² This new technology may prove invaluable for future studies of OAs.

Surgical Options

Prior to PAP methods, surgical interventions were commonly utilized as the only option to treat OSA.³ Table 5 delineates a list of common surgical procedures for OSA. With any surgical option, the patient should be informed of the risks, benefits, and alternatives. Possible side effects and complications should be explained. Surgical procedures should be considered when patients have obstructing anatomic structures that could be surgically corrected or when PAP therapy alone is insufficient.¹

Evidence supporting surgical intervention is lacking; surgical interventions compared to control, CPAP, and OAs were insufficient.¹¹ There is consensus among experts that the

best candidates for surgery are patients with known craniofacial structural abnormalities, and surgery should be performed in conjunction with CPAP treatment.¹

Bariatric surgery is recommended for any patients with BMI ≥ 40 kg/m² or BMI ≥ 30 kg/m² with significant comorbidities (e.g., T2DM, hypertension), according to the Joint Statement of American Association of Clinical Endocrinologists, the Obesity Society, and the American Society for Metabolic and Bariatric Surgery.⁴³ The AASM recommends bariatric surgery to be an adjunct to CPAP.¹ Prior to bariatric surgery, CPAP should be initiated and re-evaluated after 10% weight loss. In a study of 767 patients with untreated severe OSA with a BMI of 35-45 kg/m², 35.5% were interested in bariatric surgery.⁴⁴ Female gender and diagnosis of T2DM were most predictive of bariatric surgery interest.

Table 5. Common Surgical Procedures for OSA by Site

Nasal Procedures

Oral, Oropharyngeal, and Nasopharyngeal Procedures

- Uvulopalatopharyngoplasty & variations
- Palatal advancement pharyngoplasty
- Tonsillectomy and/or adenoidectomy
- Excision of tori mandibularis
- Palatal implants

Hypopharyngeal Procedures

- Tongue reduction
 - Partial glossectomy
 - Tongue ablation
 - Lingual tonsillectomy
- Tongue advancement/stabilization
 - Genioglossus advancement
 - Hyoid suspension
 - Mandibular advancement
 - Tongue suspension

Laryngeal Procedures

- Epiglottoplasty
- Hyoid suspension

Global Airway Procedures

- Maxillomandibular advancement
- Bariatric surgery

Table 5. Common Surgical Procedures for OSA by Site

Nasal Procedures

Adapted from: Epstein LJ, Kristo D, Stollo PJ, et al. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. *J Clin Sleep Med* 2009;5:263-276.

- Septoplasty
- Functional rhinoplasty
- Nasal valve surgery
- Turbinate reduction
- Nasal polypectomy
- Endoscopic procedure

Nocturnal Supplemental Oxygen

Studies have shown that supplemental oxygen can decrease nocturnal hypoxemia.⁴⁵ Supplemental oxygen does not reduce AHI when hypopnea is the reason for reduction in airflow. Although supplemental oxygen was more effective than control, it was less effective than CPAP for reducing AHI. Nocturnal supplemental oxygen does not lower 24-hour mean arterial pressure at 12 weeks when compared to CPAP.⁴⁶ Interestingly, adherence to supplemental oxygen was higher than CPAP in a study group of 318 participants.⁴⁶

Novel Treatments

Hypoglossal nerve stimulation therapy (HNS) has promising clinical therapeutic applications for OSA for patients who cannot tolerate or refuse to adhere to CPAP. In 1978, Remmers et al first suggested that pharyngeal obstruction was related to loss of genioglossus muscle activity in OSA patients during sleep.²⁰ A silicone cuff with electrodes is unilaterally surgically implanted around the hypoglossal nerve. The hypoglossal nerve innervates the protrusor and retractor muscles of the tongue, which are activated through continuous or synchronous stimulation from the electrodes.²⁰ Five recent trials on patients with OSA and BMI \leq 40 kg/m² showed > 50% reduction in AHI and the oxygen desaturation. Results were persistent at 12-month follow-up. A negative of the treatment was that the electrical stimulation induced arousal in patients and resulted in fragmented sleep.²⁰ More research needs to be done on the possibility of

alternate night therapy. When patients were discontinued from the therapy, the reductions in AHI and oxygen desaturation were present the following night and did not return to baseline for 5 nights.²⁰ Furthermore, questions also exist about the proportion and type of patients that might best respond to HNS and whether this is cost effective. Recent FDA approval will drive use of this treatment.¹⁵

The nasal expiratory positive airway pressure (nEPAP) device is another product that shows promise as a second-line alternative for patients intolerant of CPAP. This small plug is placed in the nose to provide pressure to the upper airway to prevent collapse. It works on the premise that at the end of expiration there is no positive pressure in the upper airway, no phasic activity of the dilator muscles, and the cross-sectional area of the upper airways is significantly narrowed.²⁰ Six clinical trials found a significant reduction in AHI and time spent snoring, and decreased oxygen desaturation.²⁰ The decreased time spent snoring may benefit patients whose sleeping partners are adversely affected by the noise of a standard CPAP machine. It also serves as a good alternative for patients who travel frequently, due to its compact size. The product is also available without a prescription, making it easily accessible to patients.

Patient Education

A Cochrane collaboration report reviewing 30 studies of patient educational, supportive, and behavioral interventions showed a positive impact on time spent using their CPAP machine in 2047 adults with OSA.²⁰ Patients should be taught basic pathophysiology and clinical consequences of OSA. A discussion regarding patient's expectations and risk factors should occur. Patients should be advised to avoid alcohol, opioids, and sedative-hypnotic medications, as they diminish respiratory drive, which can be fatal in a patient in OSA.¹ Weight loss and sleep position should also be discussed since supine position can cause an increase of apneic and hypopneic events.^{1,23}

Sleep Position

Up to 60% of patients have positional OSA, which is defined as supine AHI greater than two times that of non-supine AHI.^{20,23} The supine position changes upper airway muscles to collapse and the diaphragm to elevate. A small randomized, controlled study to

evaluate the effect of a sleep position modification device in adult participants with positional OSA (n = 47) evaluated if sleep hygiene plus the use of a position modification device (comprised of tennis balls strapped to the back) compared to the control of sleep hygiene education alone could decrease AHI.⁴⁷ After the intervention, both groups found a reduction in supine sleep. Utilization of the sleep position modification was significantly more effective than control at preventing supine sleep (mean \pm SD change from baseline, 99.5 \pm 85.2 minutes, $P = 0.002$). The proportion of total sleep time in supine was 8.7% in the study group vs 24% in the control group.

Weight Loss

Weight loss alone cannot be considered a curative treatment for OSA.⁹ If severe sleep apnea exists, a trial of weight loss is not the best choice. All patients diagnosed with severe OSA should be initiated first on CPAP. Furthermore, all patients diagnosed with OSA should be counseled on lifestyle changes.^{1,11}

In seven randomized, controlled trials comparing the impact of diet, exercise, or both on improvement in AHI and on reduction in BMI, physical activity alone did not result in AHI reduction. The combination of diet and exercise resulted in a pooled AHI reduction of 6.04 events/hour with BMI reduction of -2.32 kg/m².⁹ None of the studies demonstrated a return to normal AHI.⁹

Medications

A Cochrane review of 30 trials of 25 drugs involving 516 participants showed there was insufficient evidence to recommend the use of drug therapy of OSA.⁴⁸ The best support in research is for inhaled intranasal corticosteroids for OSA in comorbid chronic rhinitis. The intranasal corticosteroid fluticasone can help improve AHI in patients with OSA and chronic rhinitis compared to placebo (AHI 23.3 vs 30.3; $P < 0.05$).⁴⁸ Larger studies of longer duration are needed to determine the effect of intranasal corticosteroids effect of AHI change and daytime symptoms. For patients with excessive daytime somnolence with OSA, if CPAP is not resolving symptoms, modafinil can be considered adjunctive symptomatic therapy.⁴⁸ Further long-term studies on anti-obesity medications should be considered to study the impact of weight-loss on OSA.⁹

Follow-up

Primary care physicians will largely order the testing and arrange initiation of OSA treatments. In a non-inferiority, randomized, controlled study, 210 patients with OSA were randomized to be followed up at a sleep unit vs a primary care setting in Spain over a 6-month period.⁴⁹ There was no statistical difference in the compliance and blood pressure reduction in primary care vs the specialist setting. The primary care setting was more cost effective by 60%, but patients had greater levels of improvement in ESS scores and patient satisfaction in the specialty sleep unit.

The American Academy of Dental Sleep Medicine in 2013 recommends follow-up at 6 months and then annually for all OSAs.⁵⁰ Follow-up testing is not recommended for OSA patients when symptom resolution occurs with CPAP usage.¹ Follow-up visits ensure patient adherence to PAP devices. Newer PAP machines often have microchips, cards, or wireless capabilities to download user information to determine compliance. Compliance, often defined at 70% usage or approximately 4 hours per night, is often required for third-party coverage of PAP devices.

Patients who undergo bariatric surgery or those with substantial weight loss (defined by AASM as 10% of body weight) should have follow-up PSG testing.¹ A number of randomized, controlled trials investigating the impact of weight loss on severity of OSA have reported that a mean range of weight loss of 10-16% can reduce AHI by 20-50%.⁹

Complications of OSA

Moderate-severe OSA is significantly associated with all-cause mortality.³ The use of CPAP reduces mortality rates.¹⁵ Further research is needed to make associations between many comorbid disease states and OSA.

Hypertension

Sleep apnea is thought to induce inflammatory response, oxidative stress, and activation of the sympathetic nervous system, which can possibly lead to elevated blood pressure.⁵¹ In a study evaluating CPAP use over 12 weeks, nocturnal systolic blood pressure was lower for each additional hour the CPAP was used nightly.⁴⁶ In addition,

the 24-hour mean arterial pressure at 12 weeks post-intervention was lower in CPAP than control group (-2.4 mmHg; 95% CI, -5.1 to -0.5; P = 0.02).

The Wisconsin Sleep Cohort Study studied 1500 participants over 4 years showing 2.9 greater incidence of hypertension for participants with AHI > 15 vs < 5 at baseline (OR 1.5-5.6 with 95% CI).³ However, these results were not replicated in a prospective study of 2470 participants over a 5-year period.⁵² Although an increase in odds ratio for incident hypertension and increased AHI occurred, after adjusting for obesity, the association between AHI and hypertension was not statistically significant. Thus, the causative reason for developing hypertension is multi-variable and cannot be solely explained by OSA.

Diabetes Mellitus

A small study evaluated the use of CPAP machines for OSA and glycemic control in T2DM.⁵³ Patients using a CPAP for > 4 hours per night experienced a reduction of postprandial glucose and hemoglobin A1c (n = 25). The reduction of hemoglobin A1c significantly correlated with total number of days of CPAP use. The authors concluded that correcting OSA with a CPAP could have an important impact for T2DM control.

The Wisconsin Cohort Study of 1387 participants demonstrated T2DM is more prevalent in patients with sleep-disordered breathing but could not make causal inferences.⁵⁴ The Veteran Affairs Connecticut Healthcare System studied a cohort of 1233 consecutive patients and demonstrated that OSA increases the risk of developing T2DM.⁵⁵ Patients with more severe OSA that used regular PAP devices may reduce their risk of developing T2DM.

Chronic Kidney Disease

Prevalence of OSA is much greater in patients with CKD.⁵⁶ CKD may lead to OSA through fluid overload narrowing the pharyngeal structures.⁵⁷ More longitudinal studies are needed to determine the association between CKD and OSA.⁵⁶ There are no recommendations for screening CKD patients for OSA.

Cardiovascular Disease

In the Wisconsin Sleep Cohort Study, a cross-sectional study of 1500 participants determined from 4- to 15-year follow-up data that untreated sleep apnea predicted increases in hypertension, depression, cerebrovascular effects, and all-cause mortality.³ Another longitudinal study in 397 participants in Australia found a higher incidence of stroke but no significant association of cardiovascular disease or stroke.⁷ Utilizing non-CPAP treatments does not decrease mortality related to cardiovascular disease. No clear survival benefits or reductions in cardiovascular illness were associated with MADs.¹¹

Chronic Obstructive Pulmonary Disease

Coexistence of chronic obstructive pulmonary disease (COPD) and OSA, also called overlap syndrome, occurs in approximately 14% of patients with mild COPD and 11% of patients with OSA.⁵⁸ The Sleep Heart Health Study evaluated 5954 patients and did not find a significant difference in the prevalence of OSA among COPD patients and those without COPD, suggesting that COPD does not increase your risk of developing OSA.⁵⁹ However, in a recent study, 57% of patients with severe COPD requiring referral to pulmonary rehabilitation were found to have overlap syndrome.⁶⁰ It is known that overlap patients experience more nocturnal desaturations than patients with either OSA or COPD alone. When PSG results were compared between overlap syndrome patients and OSA patients, the overlap syndrome group had lower mean arterial blood saturation and spent more time in desaturation than the OSA group.⁶¹ Patients with overlap syndrome when compared to COPD patients alone were also at increased risk of death due to cardiovascular disease.¹⁴ Nasal CPAP has been associated with decreased mortality in patients with overlap syndrome.⁶² Physicians should give focused patient education in avoiding alcohol, sedative-hypnotics, opioids, and any other substance that can decrease respiratory drive.⁵⁸

Differential Diagnosis

In contrast to OSA, where airflow is disrupted because of airway obstruction, central sleep apnea (CSA) results from temporary failure of the brain to send signals to breathe. Because of the lack of respiratory effort occurring, treatment of CSA and OSA are very different. CPAP and oral devices may be contraindicated in patients with CSA,

so accurate diagnosis is important.³⁴ Investigating for other organic causes of hypersomnolence and/or insomnia, including hypothyroidism, depression, narcolepsy, restless leg syndrome, and circadian rhythm disturbances, should be ruled out. Seasonal allergies, chronic rhinitis, primary respiratory diseases, and COPD should also be evaluated in patients with loud snoring.

Further Research

Multiple areas of OSA need larger randomized controlled trials, including the impact of antiobesity medications and weight loss interventions for long-term OSA outcomes.⁹ Larger randomized, controlled trials with weight loss > 10% with long-term follow-up are necessary to understand the impact of lifestyle interventions for OSA.⁹ In addition, research focusing on the metabolic implications of OSA, including glucose regulation and cancer development, is needed. Recent studies showed glucose dysregulation and tumor growth may be related to sleep fragmentation.¹⁵ Further research is also needed in the area of perioperative sleep apnea testing. At this time there is no recommendation by the American College of Physicians or AASM for routine sleep apnea screening prior to surgery.⁴

Conclusion

The gold standard for diagnosing OSA is PSG, with CPAP as the gold standard treatment. Adherence with CPAP is variable. Consider other delivery devices and masks types, other PAP devices, surgery, oral appliances, and novel treatments when CPAP is not tolerated. Offer all patients education on lifestyle and weight loss. More randomized, controlled trials are needed to correlate comorbid conditions such as diabetes mellitus, hypertension, and cancer with OSA. Although all-cause mortality is higher in patients with OSA, there is yet to be strong clinical evidence demonstrating the causative nature of OSA on cardiovascular diseases.

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