CME

A clinical review of obstructive sleep apnea

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ABSTRACT

Symptoms of obstructive sleep apnea (OSA) often are overlooked or misinterpreted, but without treatment, patients are at increased risk for potentially life-threatening conditions including stroke and heart failure. Clinician awareness of the risk factors for and treatment of OSA can prevent the development or progression of these complications in patients.

Keywords: obstructive sleep apnea, sleep medicine, chronic disease, public health, primary care, pulmonary medicine

Learning objectives

- Define OSA.
- Correlate OSA pathophysiology to complications of untreated disease.
- Identify risk factors for OSA and indications for a sleep study.
- Describe treatments for OSA, including considerations for specific patient populations.

An estimated 9% to 38% of US adults have obstructive sleep apnea (OSA); a systematic review by Senaratna and colleagues found higher rates in men, older adults, and patients with obesity.[1] Symptoms of OSA often are overlooked or misinterpreted and include excessive daytime sleepiness, morning headaches, fatigue, fragmented sleep, witnessed apneas, snoring, and nocturnal gastroesophageal reflux. Excessive daytime sleepiness is defined as that which occurs at unwanted times and adversely affects daytime functioning.[2] Untreated, OSA can contribute to the development and/or worsening of potentially life-threatening conditions such as type 2 diabetes, coronary artery disease, hypertension, stroke, atrial fibrillation, and heart failure. Clinician awareness of patient risk factors, parameters for diagnosis, and treatment can prevent the development or progression of these complications.

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PATHOPHYSIOLOGY

OSA is characterized by recurrent and periodic partial or complete collapse of pharyngeal soft tissue during sleep, leading to periods of hypopnea and apnea despite central nervous system (CNS)-generated respiratory effort. Normal ventilation depends on unobstructed airflow through the nasal cavity, nasal valves, and pharyngeal aperture. Upper airway collapse is more likely to occur in patients with OSA than in those without the disorder, and anatomical and nonanatomical factors can contribute. Apnea is defined as cessation of breathing for 5 seconds or longer. Hypopnea carries a variety of definitions, complicating the classification of OSA, but generally is characterized by a disruption in airflow. The disruption in airflow despite respiratory muscle effort in OSA differentiates it from central sleep apnea, which is characterized by lack of CNS-generated respiratory effort.

Upper airway anatomy is a key driver of OSA; most patients with OSA have a narrowed upper airway. Narrowing can be the result of adipose deposition in the pharyngeal and parapharyngeal muscles, macroglossia, recessed mandible, webbed soft palate, septal deviations, or enlarged tonsils. These anatomy types often carry genetic predisposition and, when coupled with the loss of muscle tone during sleep, result in episodic airway collapse with resultant apneas and/or hypopneas. See **Tables 1** and **2** for additional risk factors for OSA and associated physical examination findings. Apneas and hypopneas often are more significant when patients are supine because the tongue follows gravity and falls toward the pharynx, and open-mouth breathing breaks the negative pressure seal between the tongue and hard and soft palates. Patients

Key points

- OSA is common, and its associated comorbidities can significantly impair patient health.
- The primary measure for OSA is the AHI, although it has noted limitations.
- Treatment of OSA reduces the risk of poor outcomes and includes positive airway pressure and second-line therapies for patients who cannot tolerate this traditional treatment.

TABLE 1. Risk factors for OSA[28-30]

- Family history
- Obesity
- Older age
- Male sex
- Postmenopausal state
- Use of alcohol or sedatives
- Down syndrome

TABLE 2. Physical examination findings suggestive of OSA[28]

- Septal deviation
- Scalloped tongue
- Macroglossia
- Enlarged tonsils
- Recessed mandible
- Webbed soft palate
- Neck circumference greater than 17 in (43 cm) in men or 16 in (40.6 cm) in women

may have less airway obstruction while sleeping upright (for example, in a recliner) because of this, as well as a reduction in the fluid redistribution that contributes to more crowded pharyngeal tissues while lying flat.

Regardless of the obstruction source, the pattern of disrupted ventilation results in hypoxia with resulting acute and chronic stress response. Acute swings in intrathoracic pressure as respiratory muscles work to overcome an upper airway obstruction result in atrial stretching and release of atrial natriuretic peptide (which can cause nocturia) and changes in cardiac filling pressures with an increase in myocardial oxygen demand.

COMPLICATIONS

The repeated interruptions in breathing and sleep patterns characteristic of OSA can lead to a variety of complications for patients. These complications contribute to several recognized public health burdens in the United States, including cardiovascular disease and stroke. Complications of OSA are thought to result from fragmented sleep, intermittent hypoxia and hypercapnia, intrathoracic pressure swings, and increased sympathetic nervous activity that accompanies disordered breathing during sleep.[3] These changes lead to the activation of the sympathetic nervous system, which results in vasoconstriction, increased cardiac output, and activation of the renin-angiotensin system, resulting in hypertension. Dysrhythmias may be caused by disruption of cardiac electrical activity secondary to changes in respiration, autonomic tone, and electrolyte balance.

Similar processes are implicated in the association of OSA with coronary artery disease and atherosclerosis: Increased reactive oxygen species related to chronic intermittent hypoxia result in higher levels of proinflammatory markers.[4] Additionally, intermittent hypoxia has been shown to increase insulin resistance, contributing to hyperglycemia and type 2 diabetes.[5]

Fragmented sleep with poor sleep architecture results in nonrestorative sleep, daytime somnolence, and cognitive dysfunction. The cognitive dysfunction from fragmented sleep may manifest as slower response times, lower work productivity, and strained interpersonal relationships and has been associated with higher rates of job-related accidents, motor vehicle accidents, and falls in older adults.[6,7] Patients with untreated OSA also use healthcare at higher rates than those without OSA and those with treated OSA.[8]

SCREENING

Although early identification of patients at risk for OSA is crucial to prevent or reduce associated morbidity and mortality, the US Preventive Services Task Force cites insufficient evidence to assess the benefit of screening asymptomatic patients for OSA.[9] However, the American Heart Association recommends screening in patients with cardiovascular disease, including difficult-to-treat hypertension, pulmonary hypertension, and recurrent atrial fibrillation.[10]

Routine or symptom-based screening is at the discretion of the clinician. Most simply, clinicians can ask patients (and their bed partners) about snoring, breathing pauses during sleep, excessive daytime sleepiness, morning headaches, nocturia, or sexual dysfunction. No consensus exists about specific screening tools, but several are available and in common use, including the STOP-BANG questionnaire, the Berlin Questionnaire, the Epworth Sleepiness Scale, and the NoSAS score.[11,12] The American Academy of Sleep Medicine (AASM) strongly recommends against using screening tools to diagnose OSA in the absence of a polysomnogram (PSG), citing unacceptable rates of both false-positives and false-negatives.[13] However, screening tools can help identify patients at risk of OSA who are candidates for diagnostic testing such as PSG. Use caution when interpreting the Epworth Sleepiness Scale, which only assesses sleepiness and therefore has a high specificity with lower sensitivity; this is not the best screening tool for OSA.[10,11] The

TABLE 3. Overview of screening tools for OSA[11]

	Format	Sensitivity and specificity compared with PSG	Clinical considerations
Berlin Questionnaire	Three categories with 10 questions total	• Most sensitive (97.3%) in severe OSA • Most specific (91.7%) in moderate OSA	More complex scoring method; more commonly used in research settings
STOP-BANG Questionnaire	Four subjective (snoring, tiredness, observed apnea, high BP) and four demographic (BMI, age, neck circumference, sex [referred to as gender in the acronym]) items	• Most sensitive (100%) in moderate OSA • Most specific (92.3%) in moderate OSA	Easy to administer
Epworth Sleepiness Scale	Eight items measure daytime sleepiness in Likert scale	• Most sensitive (46.1% to 79.7%) in severe OSA • Most specific (75%) in mild OSA	Sleepiness reported may be attributable to other disease states. May be used to assess response to OSA therapy.

STOP-BANG questionnaire has been demonstrated to increase the identification of patients at risk of OSA in the preoperative setting.[14] **Table 3** outlines the format, sensitivity and specificity, and clinical considerations of commonly used tools. Additional considerations for screening in the patient history and physical examination include neck circumference measurement; assessment of Mallampati score; and evaluation for history of snoring, daytime somnolence, and witnessed apnea.

DIAGNOSIS

Excessive daytime sleepiness is a common reason to consider OSA, although certainly not the only reason for this presentation. The differential diagnosis for OSA includes insufficient sleep, central sleep apnea, periodic limb movement disorder, restless leg syndrome, Kleine-Levin syndrome, structural brain lesion, fibromyalgia, depression, and sedating medications.[2] Pursue diagnostic testing for patients with clinical symptoms consistent with OSA or if the diagnosis of OSA needs to be ruled in or out as an underlying cause for another disease such as unexplained pulmonary hypertension. Diagnosis of OSA is based on clinical signs and symptoms recognized during comprehensive sleep evaluation.

The gold standard diagnostic test for OSA is laboratory-based PSG, although testing with portable monitors can be considered for patients who are unable to undergo PSG. A PSG uses a variety of metrics such as a nasal cannula with a pressure monitor to measure airflow through the nose; bands secured across the chest and abdomen to gauge respiratory effort; a pulse oximeter to measure oxygen hemoglobin saturation; a microphone to detect snoring; and an electroencephalogram, ECG, and motion detectors to assess arousal from sleep and body movement. Video equipment may be used to confirm body position and movement. A diagnostic PSG may be performed in conjunction with a titration study for positive airway pressure (PAP) therapy in a split night study; this is recommended and often preferred by patients. The AASM recommends a repeat PSG following a negative result if concern for OSA remains.[13]

Patients with concern about sleeping during a PSG should be encouraged to follow their normal sleep routine as much as possible, including sleep aids, to reproduce their typical sleep.

Patients may be candidates for home sleep apnea testing (HSAT) if they do not have significant comorbidities, such as significant cardiorespiratory disease (including heart failure or chronic obstructive pulmonary disease), respiratory muscle weakness caused by a neuromuscular condition, hypoventilation while awake or suspicion of sleep-related hypoventilation, chronic opioid use, history of stroke, or history of severe insomnia.[13] This at-home option for OSA diagnosis has been demonstrated as noninferior to PSG when comparing outcomes of treatment adherence.[15]

HSAT does not include all of the equipment typically used during PSG and cannot distinguish between when the patient is awake versus asleep, complicating interpretation. Consequently, the use of HSAT alone may underestimate the severity of OSA. For this reason, a negative or indeterminate HSAT should be followed by a PSG.[13] Because HSAT is a cost-effective method for diagnosing OSA, it is becoming more common for insurers to require an HSAT before PSG.

Either PSG or HSAT will yield an apnea-hypopnea index (AHI), the grading system used to diagnose and determine severity of OSA. An AHI is calculated by summing apneas and hypopneas per hour of sleep. An AHI of 5 to 14.9 is considered mild OSA, 15 to 29.9 is moderate, and more than 30 is severe.[13] Although AHI remains the AASM's metric of choice to stratify OSA severity, the simplicity of the calculation may under- or overestimate disease severity.[16] Calculating the frequency of apneas and hypopneas, as is done with AHI calculation, does not account for other measures that have been demonstrated

to have a significant effect on patient outcomes such as cardiovascular disease and all-cause mortality. These measures include differentiating apneas from hypopneas, duration of apneic or hypopneic events, severity and duration of oxygen desaturation, heart rate variability, awakenings, periodic limb movements, and daytime sleepiness.[16] The International Classification of Sleep Disorders has adopted the respiratory disturbance index to diagnose OSA.[17] This index includes apnea, hypopnea, and respiratory effort-related arousals per hour of sleep.

MANAGEMENT

In patients who show minimal to no symptoms, clinicians may consider lifestyle modifications, such as weight loss, oropharyngeal exercises, and positional therapy (avoiding supine sleep). The mainstay of OSA treatment is PAP to prevent airway collapse, which should be initiated in any patient with excessive daytime sleepiness or moderate to severe disease. When used regularly, PAP devices can normalize AHI and reduce OSA-related complications. The three main types of PAP devices are:

- continuous positive airway pressure (CPAP), which requires a titration study by a sleep technologist through a split night or separate titration study
- auto-titrating positive airway pressure (APAP), which adjusts pressure based on the patient's breathing patterns. Although initial titration testing is not needed, the patient does not have access to a sleep technologist for additional patient education
- bilevel positive airway pressure (BiPAP), which delivers high-pressure ventilation during inspiration and lower pressure during expiration. BiPAP may be more easily tolerated by patients, particularly those who need high-pressure levels. However, the equipment is more complex and costly than CPAP and APAP.[18]

CPAP is considered the first-line therapy for OSA, as it has been shown to improve symptoms and overall quality of life in patients who use it consistently. Further, evidence suggests patients who develop OSA after an acute stroke and begin treatment with CPAP may have improved neurologic recovery, less sleepiness, and fewer depressive symptoms.[19] Meta-analyses have shown no improvement in adherence to therapy, sleepiness, or quality of life with the use of APAP compared with CPAP after in-laboratory PAP titration.[18] Similarly, BiPAP devices provide no difference in efficacy or adherence to therapy compared with CPAP devices.[18]

Although evidence for improvement with PAP therapy is strong, patients often struggle to adhere to the therapy. Patient education and early behavioral and troubleshooting interventions are key. Patient education should include a description of OSA and the potential complications of untreated disease, how PAP therapy works, and the benefits of treatment. Closely communicate with patients starting PAP, to identify opportunities to improve adherence to therapy, such as using cognitive behavioral therapy or motivational enhancement, and to address PAP-related problems.

Adverse reactions to PAP include dry mouth, nasal symptoms, eye dryness, claustrophobia, facial pain, skin irritation, and mask leakage. Using humidified air may increase adherence in patients with dry mouth, nasal symptoms, and eye dryness. Consider pharmacologic or surgical treatment of nasal resistance or congestion, as appropriate, before starting patients on PAP.

Several measures can be used in conjunction with PAP. For patients who find that a nasal pillow mask fits well but struggle with mouth breathing, chin straps can prevent open-mouth breathing during sleep. Adipose tissue anatomy can contribute to airway obstruction and may improve with weight loss. The American Thoracic Society (ATS) recommends clinicians encourage a reduced-calorie diet and increased physical activity for patients with OSA and overweight or obesity.[20] Weight loss in patients with OSA is associated with a reduction in severity as well as an improved quality of life.[20] The ATS recommends referring to bariatrics any patient with OSA and a body mass index (BMI) greater than 35 who has been unable to lose weight with lifestyle modification.[20] Consider a referral for upper airway surgery for patients intolerant of high levels of pressure with PAP; surgical treatment of upper airway obstruction can result in lower minimum required PAP pressure and improve patient tolerability of therapy.[21] Additionally, referral for surgical evaluation may be considered for patients with upper airway anatomical variations that contribute to upper airway obstruction. The AASM recommends initiating PAP therapy for these patients before considering surgery because of the low risk of PAP therapy compared with surgery.[21] Avoiding alcohol—which affects muscle tone and can contribute to a compromised upper airway—also can reduce the AHI.[22]

Oral appliances are recommended for patients who are intolerant of PAP.[23] These devices require dentist evaluation for custom fitting and are designed to keep the airway open during sleep by protruding the tongue and mandible to facilitate increased diameter of the upper airway. Oral appliances are significantly inferior to PAP therapy in reducing the AHI for patients with severe OSA, but they may be considered for patients with mild to moderate OSA.[24] Oral appliances more often are used for snoring and are contraindicated in persons with suboptimal dental features. Research is insufficient to predict which patients are more likely to respond to oral appliance therapy. To date, female sex, younger age, lower BMI, and positional OSA have been related to successful treatment with oral appliances.[24]

Another option for patients intolerant of PAP is hypoglossal nerve stimulation. This is considered safe and effective as a second-line option for moderate to severe

OSA.[25] An implantable device detects breathing effort while stimulating the hypoglossal nerve to maintain muscle tone of the pharyngeal dilators, maintaining a patent airway while the patient sleeps. Qualifications for the device from Centers for Medicare and Medicaid Services include age 22 years or older, BMI less than 35, AHI of 15 to 65 with predominantly obstructive events, lack of complete concentric upper airway collapse with apneas (requires sleep endoscopy), PSG within 24 months of consultation, absence of anatomic features that would compromise device performance, and documented CPAP failure or intolerance.[26] Candidates for this device should be referred to a qualified otolaryngologist for further evaluation and device placement.

MONITORING AND FOLLOW-UP

The AASM recommends regular telemonitoring of PAP parameters, including device use, residual AHI on PAP, mask leaks, and other settings.[18] Follow-up also should include assessment of symptom control and monitoring for recurrence of nonrestorative sleep or daytime sleepiness despite device adherence, which may warrant alteration of equipment, settings, or a repeat PSG. Significant change in weight (gain or loss of 10% to 20%) since OSA diagnosis also is an indication for a repeat sleep study.[27] Repeat PSG also is indicated after initiating non-PAP therapy to assess response.

CONCLUSION

OSA is a common chronic condition with multiple potentially life-threatening consequences. Underdiagnosis is common, emphasizing the need for primary care providers to be aware of its risk factors, evidence-based screening, prevention, diagnosis, and management. Consider PSG evaluation in patients with excessive daytime sleepiness, particularly if the patient also has witnessed snoring and/or apneic events and underlying chronic disease such as obesity, hypertension, or diabetes. The mainstay of therapy is PAP, which requires regular use for optimal effect and can be positively affected by patient education and active management of adverse reactions. Second-line therapy options should be guided by patient-dependent factors and patient preference. Consider referral to a board-certified sleep specialist for patients with excessive daytime sleepiness and a negative sleep study or those who have persistent symptoms despite good adherence to optimized OSA therapy. Overall, identifying OSA and initiating treatment can improve quality of life and prevent or reduce comorbidities. **JAAPA**

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