

AHA SCIENTIFIC STATEMENT

Obstructive Sleep Apnea and Cardiovascular Disease

A Scientific Statement From the American Heart Association

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ABSTRACT: Obstructive sleep apnea (OSA) is characterized by recurrent complete and partial upper airway obstructive events, resulting in intermittent hypoxemia, autonomic fluctuation, and sleep fragmentation. Approximately 34% and 17% of middle-aged men and women, respectively, meet the diagnostic criteria for OSA. Sleep disturbances are common and underdiagnosed among middle-aged and older adults, and the prevalence varies by race/ethnicity, sex, and obesity status. OSA prevalence is as high as 40% to 80% in patients with hypertension, heart failure, coronary artery disease, pulmonary hypertension, atrial fibrillation, and stroke. Despite its high prevalence in patients with heart disease and the vulnerability of cardiac patients to OSA-related stressors and adverse cardiovascular outcomes, OSA is often underrecognized and undertreated in cardiovascular practice. We recommend screening for OSA in patients with resistant/poorly controlled hypertension, pulmonary hypertension, and recurrent atrial fibrillation after either cardioversion or ablation. In patients with New York Heart Association class II to IV heart failure and suspicion of sleep-disordered breathing or excessive daytime sleepiness, a formal sleep assessment is reasonable. In patients with tachy-brady syndrome or ventricular tachycardia or survivors of sudden cardiac death in whom sleep apnea is suspected after a comprehensive sleep assessment, evaluation for sleep apnea should be considered. After stroke, clinical equipoise exists with respect to screening and treatment. Patients with nocturnally occurring angina, myocardial infarction, arrhythmias, or appropriate shocks from implanted cardioverter-defibrillators may be especially likely to have comorbid sleep apnea. All patients with OSA should be considered for treatment, including behavioral modifications and weight loss as indicated. Continuous positive airway pressure should be offered to patients with severe OSA, whereas oral appliances can be considered for those with mild to moderate OSA or for continuous positive airway pressure-intolerant patients. Follow-up sleep testing should be performed to assess the effectiveness of treatment.

Key Words: AHA Scientific Statements ■ cardiovascular disease ■ clinical manifestation ■ complications ■ diagnosis ■ epidemiology ■ obstructive sleep apnea ■ therapy

Obstructive sleep apnea (OSA) is characterized by recurrent complete (apneas) and partial (hypopneas) upper airway obstructive events, resulting in intermittent hypoxemia, autonomic fluctuation, and sleep fragmentation.^{1,2} These episodic cycles of breathing disruption cause acute and chronic physiological stressors. Approximately 34% and 17% of middle-aged men and women, respectively, meet the diagnostic criteria for OSA.³ OSA prevalence is as high as 40% to 80% in patients with hypertension, heart failure (HF), coronary artery disease, pulmonary hyper-

tension (PH), atrial fibrillation (AF), and stroke.⁴ Despite its high prevalence in patients with heart disease and the vulnerability of cardiac patients to OSA-related stressors and adverse cardiovascular outcomes, OSA is often underrecognized and undertreated in cardiovascular practice.

RISK FACTORS

Male sex, older age, and obesity are established risk factors for OSA, with additional risk associated with

race/ethnicity, family history, and craniofacial dysmorphisms.⁵ The risk of OSA correlates with body mass index, and obesity remains the one major modifiable risk factor for OSA. In a population-based cohort study of 690 subjects, a 10% weight gain was associated with a nearly 32% increase in the apnea-hypopnea index (AHI), and even modest weight control was effective in reducing the new occurrence of sleep-disordered breathing.⁶ An even stronger correlation exists between OSA and increased waist circumference and neck size. Neck sizes predisposing to OSA are usually >17 and 16 in for men and women, respectively. It appears that neck circumference remains an independent predictor of OSA even after accounting for body mass index and may even provide stronger correlation with select disease severity measures such as SpO_2 nadir and AHI in patients with OSA than body mass index. Craniofacial anatomic abnormalities can narrow the upper airway and represent important risk factors for OSA that can be quantified with the modified Mallampati classification. Craniofacial abnormalities may explain the occurrence of severe OSA despite the absence of obesity as observed in Asian men. Additional less well-established risk factors include smoking, family history of OSA, and nighttime nasal congestion. Certain substances appear to exacerbate preexisting OSA but not cause it (eg, alcohol, benzodiazepines, and opiates).

PATHOPHYSIOLOGY

The pathophysiology of OSA is complex and multifactorial with many unrecognized and poorly understood facets. Overall, OSA results from the interplay between unfavorable upper airway anatomy and sleep-related alterations in airway function.⁷ Normal sleep-related physiological phenomena influence respiratory mechanics. These include, but are not limited to, reduced pharyngeal caliber, decreased muscle activity, heightened upper airway resistance, impaired respiratory load compensation, and a slight (5 mm Hg) increase in arterial carbon dioxide. Other physiologic endophenotypic factors include variations in arousal threshold, loop gain (a measure of ventilatory instability), and critical closing pressure of the airway. Morphological abnormalities are the most common factors contributing to upper airway obstruction. Examples include retrognathia, enlarged tonsils, and increased soft tissue in the neck. Notably, the distended jugular vein in patients with decompensated HF may exacerbate OSA in these patients by increasing pressure on their hypopharynx, especially while in the supine position.

CLINICAL MANIFESTATIONS

Symptoms and signs of OSA are summarized in Table 1. Additional clinical manifestations include snoring, epi-

sodes of gasping, choking, or witnessed apneas. OSA has been linked to an increased risk of job-related and motor vehicle accidents, more frequent health-related missed workdays, and decreased quality of life.⁸ Clinicians should note any abnormal cardiac or pulmonary examination findings and signs suggestive of conditions associated with an increased prevalence of OSA (eg, HF, prior stroke, AF, hypertension, diabetes).

DIAGNOSTIC EVALUATION

OSA is often suspected on the basis of symptoms and confirmed with diagnostic testing (Figure 1). Diagnostic testing can be performed by overnight in-laboratory, multichannel polysomnography, or home sleep apnea tests. Diagnosis requires the patient to have (1) reported nocturnal breathing disturbances (snoring, snorting, gasping, or breathing pauses during sleep) or symptoms of daytime sleepiness or fatigue occurring despite sufficient opportunity to sleep and unexplained by other medical conditions and (2) an AHI or Respiratory Event Index ≥ 5 . OSA may be diagnosed in the absence of symptoms if the AHI or Respiratory Event Index is ≥ 15 episodes per hour. Empirical categorization is based on AHI or Respiratory Event Index of 5 to <15 (mild), 15 to 30 (moderate), and >30 (severe).⁹ However, a singular focus on the event frequency (AHI/Respiratory Event Index) does not capture other important aspects of OSA pathophysiology such as the degree of hypoxemia, event duration, temporal distribution of events across the sleep cycle, extent of sleep fragmentation, and presence of excessive daytime sleepiness. Recent research identified hypoxia burden as a predictor for increased cardiovascular disease (CVD) risk¹⁰ with other polysomnography-derived measures (eg, loop gain, neuromuscular collapsibility) useful for identifying subgroups who may respond differently to alternative OSA treatments. Wearable technologies are progressively being adopted as diagnostic tools but need more validation.

SCREENING

OSA is widely underdiagnosed; 86% to 95% of individuals found in population surveys with clinically significant OSA report no prior OSA diagnosis.⁵ Undiagnosed cases are particularly prevalent in Black patients.¹¹ Although there is no consensus that screening for OSA in primary care clinics significantly alters clinical outcomes,¹² no study has specifically tested this question. The high prevalence and comorbidity of OSA in patients with CVD, coupled with evidence of improved patient-centered outcomes, mood, and work productivity with OSA treatment in patients with CVD,¹³ provide a rationale for OSA screening. Screening approaches include targeted elicitation of symptoms of OSA through medical history, use of screening questionnaires, or use of sleep apnea

Table 1. Diagnostic Evaluation for OSA

Diagnostic testing for OSA	Diagnostic criteria*	OSA severity classification	Comments	Novel sleep study–derived endophenotypes	Differential diagnosis
Polysomnography,* SCOPER†	AHI, standard metric Other indices: RERA contributing to RDI Percentage of sleep time with oxygen saturation <90% Nadir Sao ₂	Mild AHI ≥5–15 Moderate AHI ≥15–30 Severe AHI ≥30	Apnea: Reduction in peak signal excursion ≥90% of pre-event baseline using an oronasal thermal sensor for ≥10 s Hypopnea: Reduction in peak signal excursion ≥50% of pre-event baseline using a nasal pressure for ≥10 s with ≥3% oxygen desaturation or EEG microarousal OR if reduction in peak signal excursion ≥50% of pre-event baseline ≥4% oxygen desaturation RERA: Increasing respiratory effort for ≥10 s leading to an arousal from sleep but one that does not fulfill the criteria for a hypopnea or apnea	Sleep apnea–specific hypoxia burden (total area under the respiratory event–related desaturation curve) Loop gain (exaggerated ventilatory drive in response to reduced airflow, measured by breath-hold duration from nasal pressure signal) Respiratory arousal threshold (reduction results in small rises in ventilatory drive terminating sleep measured from nasal pressure flow signal) Increased pharyngeal collapsibility (measured from nasal pressure flow signal) Reduced pharyngeal dilator muscle effectiveness/responsiveness during sleep (measured from nasal pressure flow signal)	Hypersomnia sleep-related hypoventilation CSA Primary snoring
HSAT, standard types II–IV*	REI (scored respiratory events divided by monitoring time)	AHI=5–15 AHI ≥15–30 AHI ≥30	REI typically underestimates severity of OSA, particularly in women	As above	
HSAT, PAT	REI		Respiratory events scored by peripheral arterial tone, oxygen desaturation, and heart rate changes from oximetry	...	
Wearable devices (limited validation)	AHI surrogate indices	...	Devices with capability of collection of sleep monitoring and tracking data or sleep-related interventions	...	

Sleep studies are categorized as types I to IV with unattended studies classified as types II to IV. Type II studies use the same monitoring sensors as full polysomnographies (type I) but are unattended and therefore can be performed outside of the sleep laboratory. Type III studies use devices that measure limited cardiopulmonary parameters; 2 respiratory variables (eg, effort to breathe, airflow), oxygen saturation, and a cardiac variable (eg, heart rate or electrocardiogram). Type IV studies use devices that measure only 1 or 2 parameters, typically oxygen saturation and heart rate, or in some cases just air flow. Objective sleep testing supports the diagnosis in the context of clinical symptoms such as excessive daytime sleepiness, habitual loud snoring, witnessed apnea, or gasping or choking or diagnosed hypertension.

AHI indicates apnea hypopnea index; CSA, central sleep apnea; EEG, electroencephalography; HSAT, home sleep apnea testing; OSA, obstructive sleep apnea; PAT, peripheral arterial tonometry; RDI, Respiratory Disturbance Index; REI, Respiratory Event Index; and RERA, respiratory effort–related arousal.

*Polysomnography: electroencephalography, electrooculography, electromyography, electrocardiography, nasal thermistry, nasal pressure transducer, respiratory effort (inductance plethysmography), CO₂ monitoring (end tidal or transcutaneous), body position, video, and behaviors.

†The SCOPER classification incorporates Sleep, Cardiovascular, Oximetry, Position, Effort, and Respiratory parameters.

screening devices. A sleep history, ideally obtained with assistance from a bed partner, should include questions on frequency and severity of snoring, gasping or snorting during sleep, frequent awakening or sleep disruption, and excessive daytime sleepiness, particularly difficulty maintaining alertness, involuntary periods of dozing, or drowsy driving. Commonly used screening questionnaires include the Berlin Questionnaire, the STOP-BANG (Snoring, Tiredness, Observed Apnea, Blood Pressure, Body Mass Index, Age, Neck Circumference, and Gender), and the STOP, which include symptoms of snoring, sleepiness, and other features associated with increased OSA risk such as obesity, increased neck girth, and hypertension. These questionnaires have reported sensitivity between 77% and 89% but lower specificity (32%–34%).¹⁴ The Epworth Sleepiness Scale, which focuses on the single problem of propensity for dozing, has higher specificity (67%) but low sensitivity (42%)¹⁴ and is therefore a poor

screening tool. Screening instruments may underperform in certain groups, including women, who more commonly report fatigue and insomnia symptoms than sleepiness, and in patients with underlying CVD, HF, or AF and those after stroke.

CARDIOVASCULAR COMPLICATIONS OF OSA

OSA has been associated with a number of cardiovascular complications, including hypertension, AF and other arrhythmias, HF, coronary artery disease, stroke, PH, metabolic syndrome, diabetes, and cardiovascular mortality (Figure 2). Notably, OSA is a condition with potential for negative feedback in which it worsens conditions that may in turn worsen the OSA (eg, OSA→hypertension→worsened OSA).

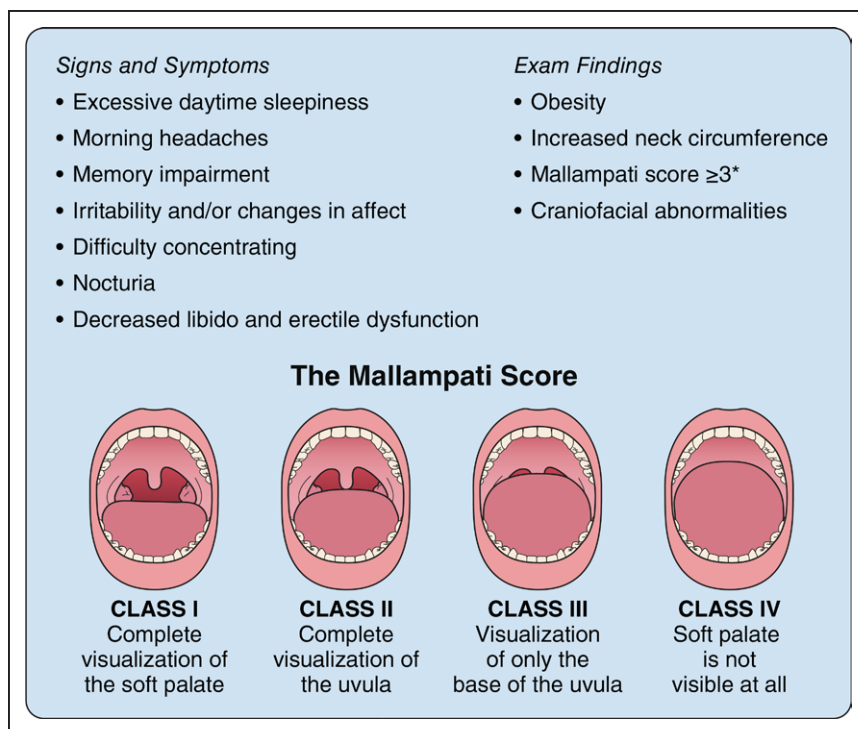


Figure 1. Obstructive sleep apnea symptoms and diagnosis.

Hypertension

OSA is highly prevalent in hypertensive patients, of whom 30% to 50% will have comorbid OSA.¹ This is especially true in patients with resistant hypertension, among whom up to 80% may have OSA.¹⁵ Although OSA has been implicated as an independent risk factor for hypertension and resistant hypertension, effects of continuous positive airway pressure (CPAP) therapy on blood pressure (BP) lowering in hypertensive patients with OSA have been disappointing and inconsistent, with a meta-analysis showing reductions of BP of between 2 and 3 mm Hg.¹⁶ CPAP adherence is associated with greater reductions in nocturnal BP. Even in patients with OSA with resistant hypertension, a 3-month treatment with CPAP (versus no CPAP) reduced 24-hour systolic, mean, and diastolic BPs by ≈ 3 mm Hg, with a significant correlation between hours of CPAP use and BP reduction.¹⁷

Notably, both OSA and hypertension are common conditions with multifactorial causes and often coexist, even though the hypertension may not necessarily be a consequence of the OSA. Non-CPAP therapies also may have a role in hypertensive patients with OSA. In a meta-analysis of oral appliance treatments (eg, soft-palate lifters, tongue-retaining devices, mandibular advancement appliances), BP reduction was similar to that noted in the meta-analysis of CPAP trials (2–3 mm Hg).¹⁸ Uvulopalatopharyngoplasty may be beneficial in selected patients, with significant decreases of 4 to 9 mm Hg reported at 6 and 24 months after surgery in a small randomized controlled trial.¹⁹ Spironolactone in a small randomized controlled trial reduced the severity of OSA and lowered

BP in patients with resistant hypertension.²⁰ In a randomized proof-of-concept study of 60 patients with resistant hypertension and moderate to severe OSA, renal denervation significantly decreased in-office and ambulatory BP at 3 and 6 months after the procedure, with modest reductions in OSA severity.²¹

Atrial Fibrillation

OSA is an independent risk factor for AF in patients without other underlying cardiac disorders.²² OSA and AF share common risk factors, including obesity, increasing age, male sex, hypertension, and HF, and are independently associated with similar adverse outcomes, but it has not been definitively proven that OSA causes AF.

There are several possible mechanisms for the substrate and trigger of AF in patients with OSA. Acute apneic episodes lead to hypoxia and hypercapnia, alteration in intrathoracic pressure, increased sympathetic tone, and autonomic dysregulation. Chronic recurrence and abrupt negative changes in intrathoracic pressure may lead to structural and functional atrial remodeling and cause atrial fibrosis with downregulation of connexin and electrophysiological alterations.²³ There is also increased incidence of extrapulmonary vein triggers, the elimination of which during AF catheter ablation can result in improvement in arrhythmia-free survival.²⁴

Multiple small and mostly retrospective observational studies have assessed the ability of CPAP to reduce AF burden after ablation or cardioversion.²³ Although limited by methodological issues and small sample size, these studies largely support the view that CPAP therapy

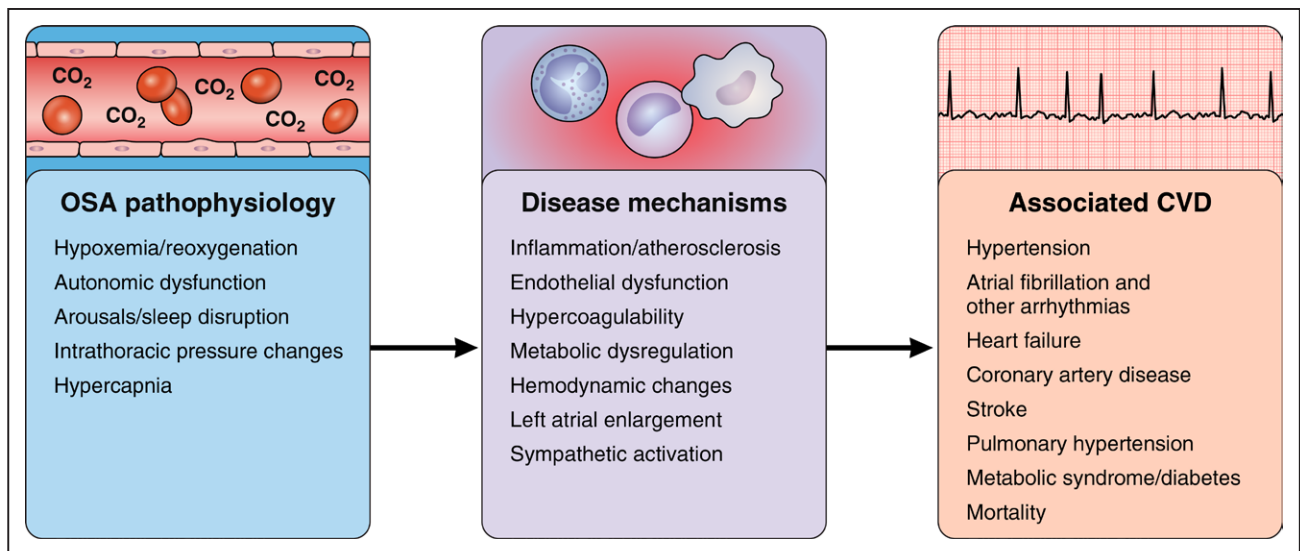


Figure 2. Cardiovascular complications of obstructive sleep apnea (OSA).

CVD indicates cardiovascular disease.

improves AF burden. This is independent of the modality for rhythm control, including antiarrhythmic drug therapy, direct current cardioversion, or catheter ablation. In a cohort of 10 132 patients with AF and OSA, patients receiving CPAP treatment were less likely to progress to permanent AF than patients without CPAP.²⁵

Future management strategies for AF should account for any accompanying sleep breathing disorder. Prospective clinical trials are required to confirm the impact of OSA on AF burden and outcomes, to clarify the benefits of OSA treatment, and to assess the need and cost-effectiveness of routine OSA screening.

Other Arrhythmias

Beyond AF, OSA is associated with a spectrum of cardiac rhythm disturbances and sudden cardiac death. Long pauses and bradycardia are common in patients with OSA. In one report, polysomnographic studies showed 58% of patients with implanted pacemakers for sick sinus syndrome had previously undiagnosed sleep apnea syndrome.²⁶ In general, patients with OSA experienced a reduction in cardiac dysrhythmias when treated with CPAP.²⁴

An increased risk of sudden cardiac death has been reported in patients with severe OSA. In a 15-year longitudinal follow-up study of 10 071 adults, OSA predicted incident sudden cardiac death, with the best predictors being age >60 years, mean nocturnal oxygen saturation <78%, and AHI >20.²⁷

Heart Failure

OSA is highly prevalent and associated with adverse outcomes in patients with HF.²⁸ Patients with HF are also at increased risk for central sleep apnea (CSA). The overall

prevalence of sleep-disordered breathing among patients with symptomatic HF is 40% to 60%, with OSA making up approximately one-third of the cases.²⁸ Most studies involving patients with HF reported roughly equal proportions of OSA and CSA. However, in a meta-analysis of 2570 patients with HF with reduced ejection fraction and moderate to severe sleep apnea, CSA represented the dominant phenotype in >70% of cases.⁴

Sleep apnea is independently associated with an increased risk of adverse outcomes, including HF-related symptom progression, hospitalization, and mortality. Patients without HF diagnosed with OSA have an increased subsequent risk of incident HF.²⁹ The pathophysiological effects of OSA relevant to HF are mediated by several mechanisms, including neurohormonal activation, increased oxidative stress and inflammation, acute increases in preload and afterload related to large intrathoracic pressure swings, and exacerbation of systemic hypertension.

Some patients such as those with obesity and HF with reduced ejection fraction may have a mixed picture of CSA and OSA. Carefully conducted and interpreted sleep studies are needed in these patients to reach an accurate diagnosis and to discern the predominant pathophysiology. Reaching the appropriate diagnosis is especially critical in patients with HF with reduced ejection fraction, given the safety concerns associated with positive pressure therapy in these patients. Although the appropriate treatment of CSA in patients with HF remains somewhat elusive, novel therapeutic approaches such as diaphragmatic stimulation and oxygen therapy are promising and rapidly evolving. Results of 2 ongoing trials, ADVENT-HF (Effect of Adaptive Servo Ventilation [ASV] on Survival and Hospital Admissions in Heart Failure) and LOFT-HF (The Impact of Low Flow Nocturnal

Oxygen Therapy on Hospital Admissions and Mortality in Patients With Heart Failure and Central Sleep Apnea), will likely inform the benefit of adaptive servo-ventilation and nocturnal oxygen supplemental, respectively, for the treatment of HF and CSA. In the context of HF, the safety and efficacy of positive airway pressure (PAP) therapies differ between patients with predominant CSA and those with OSA. CPAP appears to be only partially effective in 50% of patients with HF attributable to residual central apneas.⁷ The literature on the effects of CPAP therapy on HF outcomes among patients with isolated or predominant OSA is limited. Although several small-scale studies have reported benefits associated with CPAP, including improved left ventricular function, reduced sympathetic tone and myocardial oxygen consumption, and lower rates of HF hospitalization and mortality, a meta-analysis of patients with OSA reported that CPAP did not have significant effects on either left ventricular ejection fraction or hospitalization rates.³⁰ The 2017 American Heart Association/American College of Cardiology HF guideline identified CPAP as a possibly reasonable treatment strategy (Class IIb) to improve sleep quality and daytime sleepiness in patients with CVD and OSA.³¹

Coronary Artery Disease

OSA independently increases the risk of coronary events. The repetitive hypoxemia and reoxygenation elicited by OSA may result in oxidative stress and systemic inflammation, which contribute to coronary atherosclerosis and acute myocardial infarction (MI) events. OSA has also been implicated in coronary artery calcification, plaque instability, and plaque vulnerability and has been associated with a 2-fold increase in risk of cardiovascular events or death.³² Moore et al³³ have shown that the severity of hypoxemia is a major determinant of ST depression occurring during sleep, and in patients with OSA, the onset of MI is more likely to occur during the nighttime. Patients with ST-segment–elevation MI who also have OSA have lower 18-month event-free survival.³⁴ OSA may be implicated in an increased risk of major adverse cardiovascular events after percutaneous coronary intervention. Whether CPAP therapy decreases the risk of MI remains controversial.³⁵

Cerebrovascular Disease

A recent meta-analysis found a prevalence of post-stroke OSA of 71%, with similar findings across acute, subacute, and chronic time points.³⁶ OSA is not only an independent risk factor for incident stroke³⁷ but also an independent risk factor for stroke recurrence,³⁸ mortality, and functional and cognitive outcomes.³⁹ The association between OSA and stroke is not explained fully by hypertension or other traditional vascular risk factors and

has been posited to relate to hypercoagulability, oxidative stress, inflammation, autonomic dysfunction, paradoxical embolization, and cerebral hemodynamics. CPAP trials in patients after stroke, although challenged by treatment adherence, have shown promise for stroke recovery and secondary prevention.⁴⁰ However, clinical equipoise currently exists with respect to OSA treatment and screening after stroke, and it should be kept in mind that signs and symptoms of OSA are not predictive in patients with stroke. The ongoing Sleep for Stroke Management and Recovery Trial will likely inform the need for CPAP to improve stroke recovery and to prevent recurrence. Trials such as SAVE (Sleep Apnea Cardiovascular Endpoints), RICCADSA (Continuous Positive Airway Pressure [CPAP] Treatment in Coronary Artery Disease and Sleep Apnea), and CERCAS (Effect of Continuous Positive Airway Pressure on the Incidence of Hypertension and Cardiovascular Events in Nonsleepy Patients With Obstructive Sleep Apnea) have not provided a high level of evidence to support the benefits of CPAP for primary stroke prevention.^{4,13,35,41}

Pulmonary Hypertension

OSA is strongly associated with PH, with a reported prevalence as high as 70% to 80% among patients diagnosed with PH by right-sided heart catheterization.⁴² The primary mechanism for PH related to OSA is thought to be hypoxia-induced pulmonary arteriolar vasoconstriction mediated by signaling pathways, including nitric oxide, endothelin, angiotensin-1, serotonin, and NADPH-oxidase.⁴³ Patients with PH with OSA have increased hypoxia-induced pulmonary vascular reactivity, and CPAP treatment reduces hypoxic vascular reactivity.⁴⁴ Chronic sustained hypoxia can activate inflammatory pathways, leading to vascular remodeling and ultimately irreversible increases in pulmonary vascular resistance and right ventricular dysfunction.

PH related to OSA is generally mild in the absence of additional cardiopulmonary disease, with average mean pulmonary artery pressure between 25 and 30 mmHg and rarely exceeding 35 mmHg.⁴³ In patients with severe PH attributable to another primary cause, coexisting OSA can exacerbate the disease process and increase mortality. In contrast to isolated OSA, patients with obesity hypoventilation syndrome, which is characterized by awake hypercapnia ($P_{aCO_2} > 45$ mmHg) and obesity, commonly develop moderate to severe PH and higher risk of adverse outcomes, including cor pulmonale and death.⁴⁵

The available literature is limited by size and study design but suggests potential benefit associated with treatment of PH with CPAP. Observational studies have found consistent yet modest reductions in pulmonary artery pressure (≈ 5 mmHg) and pulmonary vascular resistance among PH patients receiving CPAP therapy.⁴⁴

Metabolic Syndrome and Type 2 Diabetes

OSA has been associated with a greater likelihood of the metabolic syndrome and type 2 diabetes, independently of adiposity level.⁴⁶ Central adiposity is linked to the development of both OSA and the metabolic syndrome, with both sharing similar pathophysiological features (eg, systemic inflammation, endothelial dysfunction).⁴⁷ In addition, intermittent hypoxia of adipose tissue, sympathetic activation, induction of adipocytokines, and oxidative stress may promote the development of metabolic risk factors.⁴⁷ Although CPAP has been shown to lower BP and markers of sympathetic activation, it has not been demonstrated to affect lipid levels, glycemic control, or rates of metabolic syndrome or diabetes.

Mortality

OSA has consistently been associated with reduced survival in epidemiological studies. A meta-analysis of 16 studies and 24 308 individuals showed that severe OSA (AHI ≥ 30) was associated with increased all-cause and cardiovascular mortality.⁴⁸ On the other hand, an association between mild or moderate OSA and increased mortality has not been found. In observational studies that examined several modalities of PAP, a significant mortality reduction was observed with PAP, with greater risk reduction observed among patients with HF.³⁰ However, large randomized controlled trials have not yet shown an effect of PAP, including CPAP, on survival.^{13,30} There are several possibilities for this discrepancy, including confounding and indication bias in observational studies, exclusion of patients with severe nocturnal hypoxemia, greater reported adherence in cohort studies, and low mortality rates with relatively limited follow-up (3–5 years) observed in clinical trials. In an analysis from the Sleep Heart Healthy Study, a PAP prescription was associated with 42% lower mortality among patients with severe OSA, but this risk reduction was not seen until 6 to 7 years of follow-up.⁴⁹ Randomized controlled trials with longer follow-up and focus on high-risk patients with severe OSA are needed to clarify the clinical benefits of PAP therapy.

TREATMENT

Numerous treatment options are available for OSA. These include CPAP, autotitrating PAP, bilevel PAP, adaptive servo-ventilation, lifestyle intervention/medical weight loss, positional therapy, oral appliances, upper airway surgery, upper airway neurostimulation, and bariatric surgery. Patients' eligibility, safety, and benefits and the estimated costs of each of these treatment modalities are summarized in Table 2.

FUTURE DIRECTIONS AND AREAS FOR RESEARCH

The widespread availability of wearable devices and remote monitoring technology provides rich opportunities for screening for the presence of sleep-disordered breathing (Table 3). The range of variables amenable to measurement include breathing, snoring, movement, heart rate, and oxygen saturation. Wearable devices have the advantage of continuous, longer-term monitoring and measurement. The rapid emergence of these technologies has outpaced robust validation studies, and their diagnostic accuracy needs to be better defined before they can be clinically adopted. Machine learning has huge potential for processing and identifying actionable data in patients with OSA and developing personalized therapies. Along these lines, home diagnostic tools need to be improved and include unobtrusive sensors for other variables (eg, electroencephalogram, electromyogram, electrooculogram). This would enable a montage of variables that replicate a complete in-laboratory polysomnogram to be acquired in the home environment on multiple nights and at a low cost.

Better cardiovascular risk stratification in the patient with OSA is important. Variables such as genotype, epigenetics, microRNA expression, and simple phenotypic measures such as sleepiness require further exploration. From a therapeutic perspective, cost-effectiveness demands better identification of which patients with OSA should be treated with the goal of preventing or mitigating CVD. As alluded to, in patients with comorbid hypertension and OSA, not all hypertension is attributable to OSA, so treatment of OSA should not necessarily be expected to consistently lower BP. A similar concept applies to other CVDs that may accompany OSA.

Innovative and effective options for therapy and evidence of risk attenuation are essential next steps in addressing the medical and economic burdens of OSA. Although CPAP has been the mainstay of therapy, this device is far from perfect and has limited adherence. Mandibular devices and neural stimulation strategies may provide viable alternatives to CPAP. Chemoreceptor modulation to attenuate OSA or its consequences is still experimental, as are pharmacologic therapeutic options for OSA.

SUMMARY RECOMMENDATIONS

Although OSA increases the risk of all-cause and cardiovascular mortality, this condition is often underrecognized and undertreated in cardiovascular practice. A strong association is present between OSA and numerous cardiovascular conditions. We recommend screening for OSA in

Table 2. Treatment Options for OSA

Treatment type	Eligibility	Effectiveness	Potential issues	Estimated costs, \$	Comments
CPAP	OSA: The Centers for Medicare & Medicaid Services cover CPAP on the basis of an AHI or REI ≥ 15 events per hour or AHI (or REI) ≥ 5 with documented symptoms of excessive daytime sleepiness, impaired cognition, mood disorders or insomnia, or documented comorbidities (ie, hypertension, ischemic heart disease, or history of stroke)	Clinical trials have shown improvement in BP, improvement in subjective sleepiness or dozing propensity (ESS), and improvement in quality of life	Pressure intolerance Mask interface issues Claustrophobia Nasal congestion Dryness of mouth or nose Skin irritation	500–1500 (typically covered in part or in full by insurer)	Targets airway collapsibility: providing constant positive inspiratory and expiratory pressure as a mechanical splint. Requires selection of pressure through an overnight laboratory titration study. 40%–80% adherence defined as use for ≥ 4 h per night for 70% of the period of use. Ramp, expiratory pressure relief, APAP may help with pressure intolerance. Heated humidification and nasal saline for nasal congestion. Clinical trial data support benefits of motivational enhancement, PAP. Nap interventions.
APAP	Same as CPAP	Trials have not consistently shown improved adherence compared with CPAP or inferiority to CPAP Improvement in BP and sleepiness	Same as CPAP	500–1500 (typically covered in part or in full by insurer)	Pressure settings are automatically adjusted with algorithms that sense change in ventilation. Can be dispensed without a prior titration study. May be useful for patients with variability in pressure needs (eg, because of positional effects). Adherence patterns and similar CPAP.
BPAP	Patients intolerant of CPAP pressure or who require additional ventilatory support	Similar to CPAP	Same as CPAP	1000–2000 (typically covered in part or in full by insurer)	Allows different pressures to be used in inspiration and expiration. May be useful for patients who do not tolerate high expiratory pressures. When combined with “backup rates,” can also be used to augment ventilation. Adherence issues similar to CPAP.
ASV	Treatment-emergent CSA in OSA in the absence of systolic HF (LVEF $< 45\%$)	SERVE-HF showed increased mortality with ASV use in those with systolic HF (LVEF $< 45\%$) and baseline central predominant sleep apnea Smaller trials have shown benefit of intermediate cardiovascular outcomes	Same as CPAP	2000–3000 (typically covered in part or in full by insurer)	Provides continuous pressure and volume adjustments to maintain constant levels of ventilation. Adherence issues similar to CPAP.
Lifestyle intervention/medical weight loss	Patients with snoring or documented OSA	10% weight loss reduces AHI by 26% Lifestyle interventions (diet, exercise, and the combination) improve OSA by similar degrees Antiobesity pharmacological therapy modestly improves OSA symptoms and severity Daytime exercise routines can prevent rostral redistribution of fluid, resulting in modest improvements in AHI	Risks of medical weight loss pharmacotherapy	2000–10 000 per year for anti-obesity pharmacotherapy	Behavioral lifestyle interventions provide a foundation for improving sleep-disordered breathing and general health and should be considered complementary approaches to more targeted OSA treatments.
Positional therapy	Indicated for positional sleep apnea defined by breathing events only (isolated) or predominantly in the supine posture often considered as supine AHI at least double the lateral AHI	Reduces AHI to the same degree as CPAP in selected patients	Discomfort leads to poor adherence	0–200 for body positioner	Long-term adherence is low (10%) ⁵⁰ because of discomfort. Newer-generation devices deliver a subtle vibrating stimulus to serve as negative reinforcement for supine sleep and associated with high short-term adherence.

(Continued)

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Table 2. Continued

Treatment type	Eligibility	Effectiveness	Potential issues	Estimated costs, \$	Comments
Oral appliances	Alternative to CPAP for mild to moderate OSA or in patients who do not tolerate CPAP	Adherence overall greater than for CPAP Comparable improvement in sleepiness Improves 24-h ambulatory BP measures and markers of inflammation	Myofascial discomfort Excess salivation	1000–2000	Includes tongue-retaining devices and mandibular advancement devices, with the latter most common. Customized devices are associated with improved outcomes compared with off-the-shelf devices. Must be prescribed by a physician and fitted by a qualified dentist.
Upper airway surgery	Multilevel surgeries are an acceptable alternative in which there are multiple levels of obstruction or collapse: nasal septoplasty, adenotonsillectomy, uvulopalatoplasty, maxillomandibular advancement	Rarely curative but may improve clinical outcomes (eg, mortality, cardiovascular risk, motor vehicle accidents, function, quality of life, symptoms)	Postoperative pain Anesthesia-related complications	10 000–100 000	Usually used in conjunction with other treatments (eg, nasal septoplasty, to improve PAP delivery) or in patients who do not tolerate or respond well to other treatments.
Neurostimulation	Adults with moderate to severe OSA (AHI 20–65 with <25% central apneas), inability to use CPAP, and lack of complete concentric collapse on DISE. Most effective in those with a BMI <32 kg/m ² ; however, those with a BMI of 32–35 kg/m ² are eligible.	Reduction in AHI Improvement in patient-reported outcomes	Invasive	30 000–40 000	Women and those who are older appear to be more responsive.
Bariatric surgery	BMI ≥35 kg/m ² and OSA as an obesity-related comorbidity	Gastric banding vs lifestyle modification provides similar benefit of improving OSA severity and symptoms OSA-specific trials have not been performed to assess the impact of bariatric procedures that result in greater weight loss, such as gastric bypass and sleeve gastrectomy, on OSA severity	Anesthesia-related risks Acid reflux Weight gain or failure to lose weight Chronic nausea and vomiting	17 000–26 000	May result in multiple metabolic benefits in addition to improved OSA. Follow-up polysomnography should be conducted to ensure resolution of OSA.

AHI indicates apnea hypopnea index; APAP, autotitrating positive airway pressure; ASV, adaptive servo-ventilation; BMI, body mass index; BP, blood pressure; BPAP, bilevel positive airway pressure; CPAP, continuous positive airway pressure; CSA, central sleep apnea; DISE, drug-induced endoscopy; ESS, Epworth Sleepiness Scale; HF, heart failure; LVEF, left ventricular ejection fraction; OSA, obstructive sleep apnea; PAP, positive airway pressure; REI, respiratory event index; and SERVE HF, Treatment of Predominant Central Sleep Apnoea by Adaptive Servo Ventilation in Patients With Heart Failure.

patients with resistant/poorly controlled hypertension, PH, and recurrent AF after either cardioversion or ablation (Table 4). In patients with New York Heart Association class II to IV HF and suspicion of sleep-disordered breathing or excessive daytime sleepiness, a formal sleep assessment is reasonable and needed to distinguish OSA from CSA. In patients with tachy-brady syndrome, those with ventricular tachycardia, or survivors of sudden cardiac death in whom sleep apnea is suspected after a comprehensive sleep assessment, evaluation for sleep apnea should be considered. After stroke, clinical equipoise exists with respect to screening and treatment. Therefore, clinical trial enrollment should be offered when possible. Patients with nocturnally occurring angina, MI, arrhythmias, or appropriate shocks from implanted cardioverter-defibrillators may be especially likely to have comorbid sleep apnea. All patients with OSA should be considered for treatment, including behavioral modifications and weight loss as indicated. CPAP should be offered to patients with severe OSA, whereas oral appliances can be considered for pa-

tients with mild to moderate OSA or for CPAP-intolerant patients. Follow-up sleep testing should be performed to assess the effectiveness of treatment.

Table 3. Future Directions and Areas for Research

More comprehensive use of wearable devices and remote monitoring technologies to provide opportunities for robust validation studies in terms of screening and treatment of sleep-disordered breathing
Use of artificial intelligence/machine learning for processing and identifying actionable data in patients with OSA and developing personalized therapies
Improvements in home diagnostic tools to include unobtrusive sensors for other variables (eg, electroencephalogram, electromyogram, electrooculogram)
Better cardiovascular risk stratification in patients with OSA
Better identification of which patients with OSA should be treated with the goal of preventing or mitigating CVD
Addressing structural racism and health inequities that undoubtedly underlie the higher prevalence and the variation in outcomes at the intersection of OSA/CVD
Innovative and effective options for therapy that are better tolerated and cost-effective

CVD indicates cardiovascular disease; and OSA, obstructive sleep apnea.

Table 4. Recommendations for Screening for OSA

Screen for OSA	Consider sleep study if concerning signs/symptoms of sleep apnea are present
Resistant/poorly controlled hypertension	NYHA class II–IV HF symptoms
Pulmonary hypertension	Tachy-brady syndrome
Recurrent atrial fibrillation (after either cardioversion or ablation)	Sick sinus syndrome
	Ventricular tachycardia
	Survivors of sudden cardiac death
	Stroke

HF indicates heart failure; NYHA, New York Heart Association; and OSA, obstructive sleep apnea.

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The American Heart Association makes every effort to avoid any actual or potential conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the writing panel. Specifically, all members of the writing group are required to complete and submit a Disclosure Questionnaire showing all such relationships that might be perceived as real or potential conflicts of interest.

Disclosures

Writing Group Disclosures

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This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives \$10,000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns \$10,000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

*Modest.

†Significant.

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