REVIEW

SILKE KRIEGER, MD
Department of General Internal Medicine, Cleveland Clinic

SEAN M. CAPLES, DO
Assistant Professor of Medicine, Division of Pulmonary and Critical Care Medicine, Mayo Clinic, Rochester, MN

Obstructive sleep apnea and cardiovascular disease: Implications for clinical practice

ABSTRACT

Obstructive sleep apnea is common, underdiagnosed, undertreated, and highly associated with cardiovascular risk. It is characterized by daytime sleepiness and disrupted sleep and is confirmed by overnight sleep studies (polysomnography). Treatment with continuous positive airway pressure (CPAP) improves sleep and daytime sleepiness, but its effects on cardiovascular risk, while promising, are still unclear.

KEY POINTS

CPAP is the most effective treatment for obstructive sleep apnea and is available in several different delivery systems.

For patients with obstructive sleep apnea, CPAP may lower blood pressure in those with daytime sleepiness, improve left ventricular ejection fraction in those with heart failure, and reduce cardiovascular risk.

Strokes and transient ischemic attacks share risk factors with obstructive sleep apnea, but whether sleep apnea is an independent risk factor for ischemic cerebrovascular disease has not been proven.

Upper airway surgery could be considered for patients unable to tolerate CPAP, but available data regarding efficacy are limited.

OBSTRUCTIVE SLEEP APNEA is strongly associated with cardiovascular disease, but whether the association is causal is difficult to prove. Because mild to moderate obstructive sleep apnea is common, determining who would benefit from therapy remains a key question.

This article discusses the clinical presentation, diagnosis, and treatment of obstructive sleep apnea and reviews recent literature on its association with cardiovascular disease.

OBSTRUCTIVE SLEEP APNEA IS COMMON

Obstructive sleep apnea is the most common sleep-related breathing disorder and is widely recognized as a public health problem.[1] In the United States, it is more prevalent than asthma and is as common as diabetes mellitus.[2,3]

In the Wisconsin Sleep Cohort Study,[4] when 602 randomly selected employed men and women aged 30 to 60 years underwent polysomnography, 9% of the women and 24% of the men had an abnormal apnea-hypopnea index (AHI; see below). Furthermore, 4% of the men and 2% of the women had both an abnormal AHI and sleep apnea-related symptoms.

Overweight, older people most at risk

Risk factors for obstructive sleep apnea include excess weight, male sex, and advanced age.[5–7] It is most common between the fifth and seventh decades.[7,8] Menopause significantly increases the risk for obstructive sleep apnea independently of other factors; after

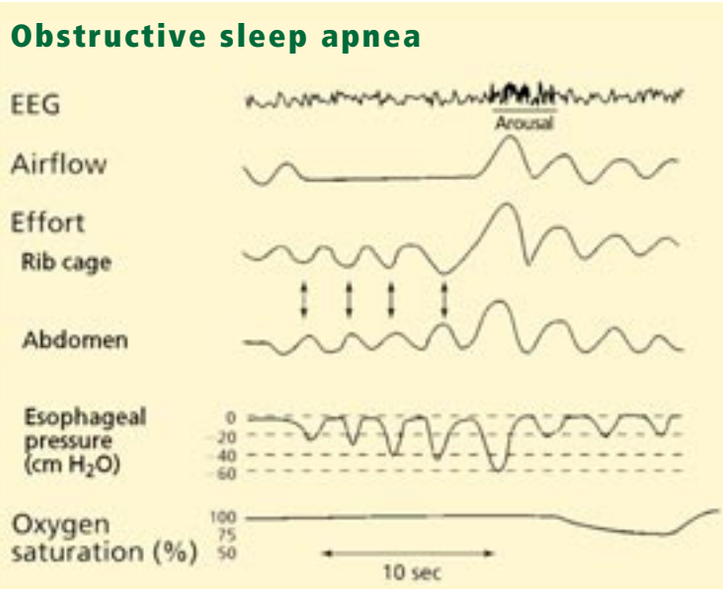

FIGURE 1. Polysomnographic recording of obstructive sleep apnea depicting paradoxical rib cage and abdominal movements with cessation of oronasal flow. Note swings in intrathoracic pressure as measured by esophageal pressure. Arousal on the electroencephalogram (EEG) is associated with a gasp and resumed ventilation. Oxyhemoglobin desaturation is seen later because of circulatory delay from the chest to the peripherally located oximeter probe.

ADAPTED FROM STROLLO PJ JR, ROGERS RM. OBSTRUCTIVE SLEEP APNEA. N ENGL J MED 1996; 334:99–104.

menopause, women develop obstructive sleep apnea at a rate similar to that in men.[9]

Obesity, the most important risk factor, exists in approximately 70% of patients with obstructive sleep apnea.[10,11] Certain craniofacial and upper airway anatomic features, which may be more common in Asians, also predispose to the condition.[12]

APNEA DUE TO UPPER AIRWAY CLOSURE

Respiratory events during sleep in adults have been scored by the same criteria for more than 30 years[13] but are now being examined by the American Academy of Sleep Medicine for possible revision. By current definitions, disordered breathing events are associated with cessation (apneas) or reduction (hypopneas) in measurable airflow as well as a minimum 4% drop in oxyhemoglobin saturation.

Apnea and obstructive hypopnea frequently occur in the same patient. They result from reduced airflow during sleep due to partial or complete occlusion of the upper airway at the oropharyngeal level. The respiratory pump continues to generate breathing efforts against an occlusion, resulting in paradoxical movements of the chest wall and abdomen as well as swings in intrathoracic pressure (as measured by an esophageal balloon, since esophageal pressure is a surrogate of intrathoracic pressure) (FIGURE 1).[14]

How obstructive sleep apnea develops is complex and involves anatomic, genetic, and environmental factors. Narrowing or closure may occur at one or more sites in an unstable upper airway and is influenced by neuromuscular tone, compliance of the pharynx, upper airway muscle synchrony, and stage of sleep. Upper airway size and patency are anatomically determined by soft tissue and skeletal factors. In obese patients, the lumen of the pharynx is narrowed by nearby fat-layering. Hypertrophy of the tonsils and enlarged lateral pharyngeal walls also predispose to airway narrowing during sleep.[15]

SYMPTOMS: DAYTIME SLEEPINESS, DISRUPTED SLEEP

In the United States, obstructive sleep apnea is estimated to be undiagnosed in 75% to 80% of people who could benefit from treatment.[16] Primary care physicians are in a unique position to identify and evaluate these patients.

Most high-risk patients do not fit the stereotype of Pickwickian syndrome (ie, extreme obesity and excessive sleepiness).[6] The term "Pickwickian syndrome" is outdated and has been supplanted by "obesity-hypoventilation syndrome," which is characterized by chronic hypoventilation and hypercapnia during wakefulness.[17,18] Large, population-based cohorts have found that the typical patient with obstructive sleep apnea has a body mass index of between 28 and 32 kg/m^2.

Probably the best ways to identify patients likely to have obstructive sleep apnea are to ask patients about their quality of sleep and daytime sleepiness and to seek additional history from others. Commonly, the bed partner reports loud snoring with brief gasps alternating with episodes of silence lasting 20 to 30 seconds.

Patients typically complain of daytime somnolence with drowsiness, particularly during "permissive situations" (eg, after meals, while watching television, or attending a lecture). A sensation of choking that interrupts sleep, nocturnal palpitations, restlessness with frequent turning, esophageal reflux, and dryness of mouth are also frequently reported.[19] Dull headaches occurring in the morning or at night are occasionally reported.

Cognitive impairment—including attention deficit, memory decline, and impaired concentration and judgment—has been associated with obstructive sleep apnea and in some cases may be reversible with continuous positive airway pressure (CPAP) treatment.

The initial physical examination should focus on cardiorespiratory, endocrine, and metabolic disease and abnormalities of the upper airway structure. Obesity, craniofacial abnormalities, symptomatic hypothyroidism, and acromegaly should raise the suspicion of obstructive sleep apnea.

Combinations of clinical variables such as body mass index, snoring, reports of nocturnal breathing disturbances, adjusted neck circumference, and a history of hypertension have been used in primary care settings to predict abnormal sleep-test results.[20] Screening questionnaires such as the Epworth Sleepiness Scale[21] or the Berlin questionnaire are more formal predictors but do not substitute for directly measuring breathing during sleep.[22] The usefulness of methods such as overnight pulse oximetry for screening has not been proven.

POLYSOMNOGRAPHY IS NEEDED FOR DIAGNOSIS

To diagnose obstructive sleep apnea and assess its severity, current guidelines recommend performing full overnight sleep studies with polysomnography.[23] The role of ambulatory in-home monitoring is evolving but is not currently standard for the diagnosis of obstructive sleep apnea in the United States.

Polysomnography entails the simultaneous recording of several variables for staging and quantifying sleep as well as for identifying sleep arousals or awakenings. The test includes:

- **Standard respiratory measurements,** including arterial oxygen saturation by ear or finger pulse oximetry
- **Recordings of chest and abdominal excursions** to detect apneas or hypopneas and classify them as obstructive and nonobstructive
- **Electrocardiography** to monitor heart rhythm
- **Surface electromyography** to monitor skeletal muscle activity (typically jaw and leg movements are recorded)
- **Electroencephalography** to measure brain electrical activity
- **Electro-oculography** to measure eye movements and determine when sleep occurs, as well as when the rapid eye movement stage occurs.

The apnea-hypopnea index

The apnea-hypopnea index (AHI) is the number of episodes of apnea (cessation of breathing) and hypopnea (breathing that is slower or shallower than normal) per hour of sleep.[24] Results are classified as:

- < 5—normal
- 5–14—mild apnea
- 15–29—moderate apnea
- ≥ 30—severe apnea.

Patients with very severe obstructive-sleep apnea may have an AHI exceeding 100.

However, the AHI is imperfect because it does not incorporate all the important variables, such as the number of arousals from sleep, which may be most critical in a patient with daytime sleepiness, or the degree of oxygen desaturation, which may have the most impact on outcome in severe coronary artery disease.

Poor sleep and daytime sleepiness help identify patients likely to have obstructive sleep apnea

Polysomnography helps distinguish obstructive sleep apnea from other sleep-related breathing disorders such as simple snoring, circadian rhythm disorder, central sleep apnea, narcolepsy, and periodic limb movement disorder.

CARDIOVASCULAR DISEASE IS ASSOCIATED WITH SLEEP APNEA

Evidence is increasing that obstructive sleep apnea is associated with common vascular disorders including hypertension, heart failure,

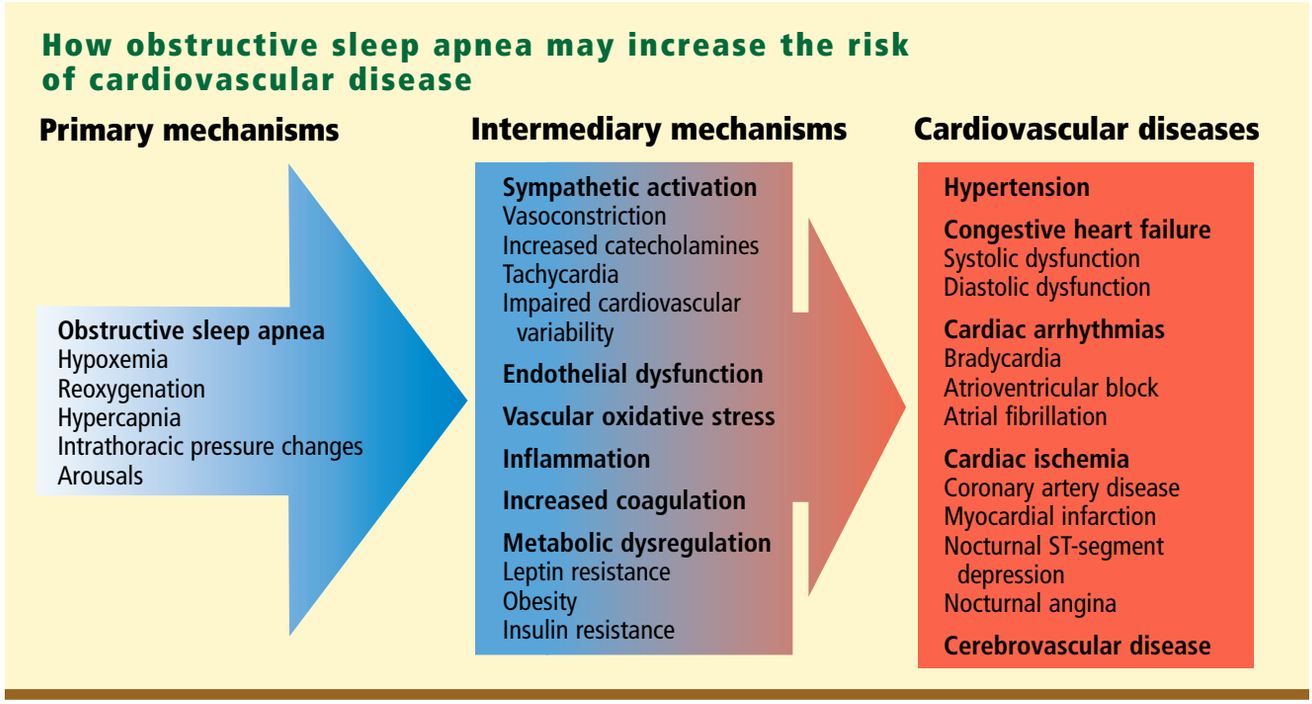

FIGURE 2. Abnormalities associated with obstructive sleep apnea may be intermediary mechanisms that contribute to the initiation and progression of cardiac and vascular pathology. These mechanisms may interact with each other, thus potentiating their pathophysiologic implications.

SHAMSUZZAMAN AS, GERSH BJ, SOMERS VK. OBSTRUCTIVE SLEEP APNEA: IMPLICATIONS FOR CARDIAC AND VASCULAR DISEASE. JAMA 2003; 290:1906–1914.

If obstructive sleep apnea causes cardiovascular disease, CPAP could reduce death and disease

myocardial infarction, and stroke. However, proving that obstructive sleep apnea actually causes cardiovascular disease independent of confounding risk factors is difficult. For example, obesity is a risk factor for obstructive sleep apnea and cardiovascular disease, and both problems often exist in the same patient.

The question whether obstructive sleep apnea causes cardiovascular disease is important, because if it does, treating it with CPAP could reduce death and disease from major cardiovascular and cerebrovascular events. However, evidence from large randomized controlled trials is lacking, and results of cohort studies and small trials have been conflicting.

Obstructive sleep apnea may increase the risk of cardiovascular risk via a number of different mechanisms (FIGURE 2).[25]

Hypertension is increased

Patients with obstructive sleep apnea have higher average blood pressure than do age- and sex-matched controls.

The recent Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure lists obstructive sleep apnea as an identifiable cause of hypertension.[26]

A number of events that occur during obstructive sleep apnea could contribute to blood pressure elevations. Respiration significantly influences the short-term modulation of sympathetic nerve activity: repetitive hypoxemia from episodes of apnea and hypopnea stimulates peripheral chemoreceptors, located at the carotid bifurcations, resulting in reproducible phasic increases in sympathetic neural output as well as an increase in sympathetic tone.[27] Repetitive hypoxia and arousal further increase sympathetic tone[28] and are thought to be key to short-term and long-term blood pressure elevations. Obstructive sleep apnea is also associated with impaired endothelium-dependent vasodilatation of resistance vessels.[29]

Fletcher et al[30] exposed rats to 35 days of chronic intermittent hypoxia (simulating the pattern found in obstructive sleep apnea) and found that mean arterial blood pressure increased 13.7 mm Hg. Brooks et al[31] exposed

dogs to recurrent airway occlusion during sleep. Acute transient increases occurred in nighttime blood pressure, and within 4 weeks, daytime blood pressure increased.

The first convincing evidence in humans of an independent relationship between obstructive sleep apnea and sustained daytime hypertension was from the prospective, population-based Wisconsin Sleep Cohort Study.[32] Adults with a baseline AHI of 15 or more had nearly three times the risk of developing hypertension 4 years later. Risk increased with a higher AHI; even minimal sleep-disordered breathing increased risk. The association was independent of body habitus, age, sex, and cigarette and alcohol use. A possible limitation of this study was the inclusion of subjects with treated hypertension at baseline.

The Sleep Heart Health Study,[33] a cross-sectional analysis of 6,132 healthy middle-aged and older adults, found that sleep-disordered breathing was associated with hypertension, independent of possible confounders including body mass index, fat distribution, alcohol intake, and smoking.

These studies provide strong evidence for an association between elevated blood pressure and obstructive sleep apnea. However, a definitive cause cannot be established from cross-sectional studies, because they are potentially affected by selection and prevalence-incidence bias.

CPAP is the most immediately effective treatment for obstructive sleep apnea

CPAP lowers blood pressure in some cases

Standard treatment with CPAP acutely lowers sympathetic drive and nocturnal blood pressure in patients with obstructive sleep apnea.[34,35] But data supporting an effect of CPAP on daytime blood pressure are variable. Even results from randomized controlled trials can be difficult to interpret: baseline differences in study subjects and variable study methods may contribute to inconsistent outcomes.

While the relationship between obstructive sleep apnea and blood pressure is complex, two important determinants of the blood pressure response to CPAP treatment have emerged: excessive daytime sleepiness and baseline blood pressure.

Barbe et al[36] found that in patients with severe obstructive sleep apnea by AHI criteria with generally normal blood pressure and without subjective sleepiness, blood pressure did not significantly change after 6 weeks of CPAP therapy.

Robinson et al[37] found that patients with obstructive sleep apnea with elevated blood pressure but without daytime sleepiness did not have significantly lower blood pressure after 1 month of CPAP treatment.

Campos-Rodriguez et al[38] found no significant changes in blood pressure after 4 weeks of CPAP in patients with obstructive sleep apnea with modest daytime sleepiness who were already being treated for hypertension.

However, Pepperell et al[39] found that in patients with marked daytime sleepiness (mean Epworth Sleepiness Scale score 16) and slightly elevated baseline blood pressure levels, blood pressure was significantly reduced after a month of CPAP therapy.

Moreover, Becker et al[40] found the largest blood pressure reductions in sleepy patients (mean Epworth Sleepiness Scale score 14) with very severe sleep apnea (AHI > 60). (Most patients were being treated for hypertension before the study, and no change in hypertension therapy was allowed during the study.)

These data suggest that CPAP lowers blood pressure in some patients with obstructive sleep apnea, particularly those with daytime sleepiness, but not in those with mild apnea or even severe disease with only minimal clinical symptoms.

Congestive heart failure is increased

Patients with heart failure commonly have either central or obstructive sleep apnea, and increasing evidence indicates that both forms of sleep-disordered breathing share some common pathophysiologic mechanisms.[41,42]

Sin et al,[43] in a retrospective study of 450 patients with congestive heart failure who were referred to a sleep laboratory, found that the prevalence of obstructive sleep apnea was 32%. Chan et al[44] found that half of patients with isolated diastolic heart failure had an abnormal AHI. The Sleep Heart Health Study[45] found that obstructive sleep apnea is associated with significantly increased odds of having heart failure. Experimental evidence also indicates that heart failure may predispose to obstructive sleep apnea, possibly

because of upper airway soft tissue edema.[46]

Few interventional trials have evaluated the effect on heart failure of treating obstructive sleep apnea. Mansfield et al,[47] in a randomized controlled therapeutic trial in patients with stable heart failure and obstructive sleep apnea, found that 3 months of nocturnal CPAP was associated with significantly improved left ventricular ejection fraction. Kaneko et al[48] found similar improvements in patients with ischemic and nonischemic dilated cardiomyopathy treated with 1 month of CPAP. Interestingly, even though they had severe obstructive sleep apnea as measured by the AHI, the patients in both studies reported only mild daytime sleepiness.

Further research is needed to determine the impact of CPAP on cardiovascular outcomes in heart failure, particularly for patients who report no significant daytime sleepiness.

Coronary artery disease is increased

Ample experimental and observational data suggest that obstructive sleep apnea is an important risk factor for vascular disease.

Hypoxemia, postapneic reoxygenation, hypercapnia, sympathetic activation, acute pulmonary hypertension, and surges in blood pressure are potent stimuli for the release of vasoactive substances and for impaired endothelial function. Neutrophils and monocytes increase production of reactive oxygen species, and expression of adhesion molecules and cytokines (interleukin 6, tumor necrosis factor alpha) is enhanced. Many patients have elevated C-reactive protein levels.[25]

Obstructive sleep apnea increases the risk of fasting hyperglycemia, insulin resistance, and type 2 diabetes mellitus.[49] Hanly et al[50] performed overnight electrocardiography in patients with obstructive sleep apnea who were free of clinically significant coronary artery disease and found that ST-segment changes occur during respiratory events.

Despite this strong association, randomized controlled interventional trials have failed to show that treating obstructive sleep apnea improves cardiovascular risk beyond small reductions in blood pressure in some patients. However, such studies are prone to a myriad of methodologic challenges.

Marin et al,[51] in a recent 10-year cohort study, compared the incidence of fatal and nonfatal cardiovascular events in healthy men, simple snorers, patients with untreated obstructive sleep apnea, and patients treated with CPAP. Multivariate analysis adjusted for potential confounders showed that patients with untreated severe obstructive sleep apnea had a significantly increased risk of fatal and nonfatal cardiovascular events vs subjects in all other groups (odds ratio 2.87 and 3.17, respectively). The risk of cardiovascular events was associated with the severity of untreated sleep apnea. CPAP treatment for at least 4 hours per night significantly reduced cardiovascular risk. While the observational nature of the study and some baseline differences between groups may bias the results, the length of this study strengthens the evidence that CPAP treatment reduces long-term cardiovascular risk.

Risk of stroke is increased

Strokes and transient ischemic attacks share risk factors with obstructive sleep apnea, but whether sleep apnea is an independent risk factor for these events has not been proven. Sleep-related breathing disorders are both a possible risk factor and a consequence of stroke.[52,53] Sleep apnea is very common following stroke (60%–70%) and is independent of neurologic recovery.[54] A case-control study showed no increased rate of obstructive sleep apnea in patients with transient ischemic attacks when compared with controls.[55]

Yaggi et al,[56] in an observational cohort study, followed patients who were referred to a sleep center over a median of 3.4 years and found an increased risk of stroke or death among patients with obstructive sleep apnea, with more severe apnea associated with greater risk. No effect on outcomes was found from various therapies (CPAP, weight loss, upper airway surgery), but the study was not designed to assess treatment.

Further longitudinal interventional studies are needed to assess the effect of apnea treatment on cerebrovascular disease.

People with sleep apnea are more likely to be involved in motor vehicle accidents

A PROPENSITY FOR ACCIDENTS

Drowsiness itself is an important risk factor for injury and death; evidence indicates that

TABLE 1

General approach to managing obstructive sleep apnea

Assess indications for treatment
Disease severity
Reasons for referral and patient goals
Surgically correctable upper airway abnormalities (eg, tonsillar hypertrophy)
Symptoms and other medical conditions

Lifestyle modification
Avoidance of alcohol and sedatives
Avoidance of caffeine and daytime naps
Lateral sleep position
Smoking cessation
Weight loss

Adjunctive therapy
Relief of nasal obstruction (intranasal medication or surgery)

Nasal continuous positive airway pressure (CPAP) indicated for:
Coexisting cardiovascular disease
Hypersomnolence
Moderate to severe obstructive sleep apnea

Oral appliance therapy for:
Mild to moderate obstructive sleep apnea if not morbidly obese
Patients unable or unwilling to use CPAP

Corrective upper airway surgery for:
Clearly defined locus of upper airway obstruction
Patients with no significant comorbidities
Treatment failures with nasal CPAP and oral appliance therapy

ADAPTED FROM RYAN CF. SLEEP • 9: AN APPROACH TO TREATMENT OF OBSTRUCTIVE SLEEP APNOEA/HYPOPNOEA SYNDROME INCLUDING UPPER AIRWAY SURGERY. THORAX 2005; 60:595–604

patients with sleep apnea are more likely to be involved in motor vehicle accidents.[57,58]

TREATMENT

Several options are available for treating obstructive sleep apnea (TABLE 1),[59] although no drug has proven effective.

CPAP is the most effective treatment

Supported by more than 2 decades of use, CPAP is without a doubt the most immediately effective treatment for obstructive sleep apnea and is the standard of care for moderate to severe disease.[60]

Patients with daytime symptoms attributable to obstructive sleep apnea should be offered a trial of CPAP and informed that it must be used continuously during sleep, that full benefit may not be realized for several weeks, and that it does not offer a cure.

Delivered by nasal or oronasal mask, CPAP provides a pneumatic stent of the upper airway, preventing collapse and increasing airflow while eliminating snoring. Sleep continuity improves and respiratory arousals are reduced.

Optimal treatment pressure can be determined in a sleep laboratory titration study. Alternatively, an autotitrating device may be acceptable in some circumstances.[61] Pressure requirements may change over time, but appropriate follow-up intervals have not been determined. Weight loss or gain may respectively reduce or increase the therapeutic pressure required. In addition, disease severity tends to increase with age, and patients who have been stable for several years with a given pressure may develop breakthrough apnea events.

Despite CPAP's effectiveness, many patients find it difficult to tolerate and adhere to therapy. Experimenting with different devices may help: masks are available in a variety of sizes, shapes, and materials, and nasal pillows can be used as an alternative. A chin strap or an oronasal mask may help if a persistent air leak through the mouth is a problem. Nasopharyngeal congestion and rhinorrhea are common side effects, which may be helped by humidifying the delivered gas, applying topical nasal steroids, or using ipratropium spray (Atrovent).

Other forms of PAP that may prove useful, particularly if laboratory titration of CPAP is unsuccessful, include bi-level assisted ventilation (BiPAP) and autotitrating PAP devices.

Weight loss, other conservative measures

Weight loss should be recommended to all overweight patients diagnosed with obstructive sleep apnea. Even modest weight loss can help, and dramatic weight reduction, such as after bariatric surgery, may completely eliminate the problem.[62]

Patients with mild disease may be primarily treated with general measures, including avoiding alcohol and other central nervous system depressants, treating nasal congestion,

changing from a supine to a lateral sleep position, and avoiding sleep deprivation. Patients should also avoid caffeine and other stimulants, maintain a regular sleep-wake schedule, and avoid daytime napping. Environmental changes may help promote a comfortable undisturbed sleep.

Patients should be counseled to quit smoking, although evidence linking cigarette smoking with obstructive sleep apnea is circumstantial.

Supplemental oxygen can help patients with chronic lung disease who have significant arterial oxygen desaturation during sleep.

Perhaps the upper airway muscles can be trained. A recent randomized controlled trial found that patients with moderate obstructive sleep apnea and snoring who regularly played a didgeridoo (an Australian wind instrument) for 4 months had moderately reduced AHI and symptoms.[63]

Oral appliances can help

Oral appliances move the tongue or mandible forward to increase upper airway caliber. An experienced dental specialist or orthodontist can create a reasonable alternative treatment for patients with mild to moderate disease who do not benefit from CPAP or cannot tolerate it. Regular follow-up and objective testing, which may include polysomnography, are critical to ensure efficacy.

Trying different masks may help patients tolerate CPAP

Upper airway surgery can be an alternative

The benefits of upper airway surgery have not been proven by randomized trials or long-term observational studies and should be considered only for patients who cannot tolerate or who refuse CPAP therapy. Young patients in particular may prefer surgery over long-term CPAP therapy.

Procedures include uvulopalatopharyngoplasty, laser-assisted uvulopalatoplasty, tonsillectomy, partial resection or ablation of the tongue, reconstruction of the mandible or maxillae, and tracheostomy. These should be performed only by experienced surgeons.

Uvulopalatopharyngoplasty has been performed for decades, but benefits tend to wane with time. Complications may include pain, bleeding, nasopharyngeal stenosis, changes in voice, and death.[64]

Soft palatal implants are undergoing clinical trials to assess their efficacy in mild to moderate obstructive sleep apnea.

Tracheostomy is a viable treatment in those with refractory disease but is much less frequently employed than in past years.

Cardiac overdrive pacing is unproven

Cardiac overdrive pacing was proposed as a treatment for obstructive sleep apnea based on a preliminary trial,[65] but a follow-up trial found it ineffective.[66] Cardiac pacing may reduce the occurrence of *central* apneas through its effects on feedback to the central respiratory centers and may one day play a role in treating this condition.[67]

PERIOPERATIVE CONSIDERATIONS

Because of chronic sleep disruption and a propensity for upper airway collapse, patients with obstructive sleep apnea are at high risk of exaggerated disordered breathing during anesthesia. Postoperative effects of anesthesia and surgery have produced apnea even in patients without a history of sleep-disordered breathing.[68]

Only limited data exist on the adverse effects of obstructive sleep apnea on postoperative outcomes. Several case reports and a retrospective case-control study[69] noted a higher risk of perioperative complications in patients with obstructive sleep apnea than in matched controls. Because obstructive sleep apnea is associated with multiple medical and vascular conditions, preoperatively diagnosing and treating the condition may reduce the risk of adverse postoperative outcomes, but data are lacking. Risk may be especially high for surgical patients who have obstructive sleep apnea that has never been diagnosed.

The American Society of Anesthesiologists recently published guidelines for the perioperative management of patients with obstructive sleep apnea.[70] Despite the lack of data upon which to base recommendations, consensus was reached on a few important points. A formal protocol should be developed by a multidisciplinary group of health care providers (surgeons, anesthesiologists, and primary care physicians) to identify patients at risk of obstructive sleep apnea and to institute

appropriate perioperative measures. Regional or peripheral anesthesia should be considered when possible. Postoperative management may include close monitoring (perhaps in an intensive care or step-down unit), nonsupine positioning when possible, and supplemental oxygen. If monitoring confirms apneas, empiric CPAP therapy may be applied, although further study is needed to prove efficacy.

We recommend the continued use of CPAP in surgical patients with a previous diagnosis of obstructive sleep apnea, and we encourage patients to bring their device to the hospital. Observational studies suggest that the perioperative use of CPAP reduces the risk of postoperative complications.[69,71]

REFERENCES

1. **Lacasse Y, Godbout C, Series F.** Health-related quality of life in obstructive sleep apnoea. Eur Respir J 2002; 19:499–503.
2. **Kuna ST.** A 54-year-old man with obstructive sleep apnea. JAMA 2002; 288:2032–2039.
3. **Harris MI, Flegal KM, Cowie CC, et al.** Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in U.S. adults. The Third National Health and Nutrition Examination Survey, 1988–1994. Diabetes Care 1998; 21:518–524.
4. **Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S.** The occurrence of sleep-disordered breathing among middle-aged adults. N Engl J Med 1993; 328:1230–1235.
5. **Punjabi NM, Polotsky VY.** Disorders of glucose metabolism in sleep apnea. J Appl Physiol 2005; 99:1998–2007.
6. **Young T, Skatrud J, Peppard PE.** Risk factors for obstructive sleep apnea in adults. JAMA 2004; 291:2013–2016.
7. **Redline S, Tishler PV, Tosteson TD, et al.** The familial aggregation of obstructive sleep apnea. Am J Respir Crit Care Med 1995; 151:682–687.
8. **Young T, Peppard PE, Gottlieb DJ.** Epidemiology of obstructive sleep apnea: a population health perspective. Am J Respir Crit Care Med 2002; 165:1217–1239.
9. **Coleman RM, Roffwarg HP, Kennedy SJ, et al.** Sleep-wake disorders based on a polysomnographic diagnosis. A national cooperative study. JAMA 1982; 247:997–1003.
10. **Malhotra A, White DP.** Obstructive sleep apnoea. Lancet 2002; 360:237–245.
11. **Benumof JL.** Obstructive sleep apnea in the adult obese patient: implications for airway management. Anesthesiol Clin North Am 2002; 20:789–811.
12. **Li KK, Kushida C, Powell NB, Riley RW, Guilleminault C.** Obstructive sleep apnea syndrome: a comparison between Far-East Asian and white men. Laryngoscope 2000; 110:1689–1693.
13. **Rechtschaffen A, Kales A, editors.** A Manual of Standardized Terminology Techniques and Scoring system for Sleep Stages of Human Subjects. Bethesda, MD: US Dept of Health, Education, and Welfare; 1968.
14. **Strollo PJ Jr, Rogers RM.** Obstructive sleep apnea. N Engl J Med 1996; 334:99–104.
15. **Schellenberg JB, Maislin G.** Schwab RJ. Physical findings and the risk for obstructive sleep apnea. The importance of oropharyngeal structures. Am J Respir Crit Care Med 2000; 162:740–748.
16. **Kapur V, Strohl KP, Redline S, Iber C, O'Connor G, Nieto J.** Underdiagnosis of sleep apnea syndrome in U.S. communities. Sleep Breath 2002; 6:49–54.
17. **Bickelmann AG, Burwell CS, Robin ED, Whaley RD.** Extreme obesity associated with alveolar hypoventilation; a Pickwickian syndrome. Am J Med 1956; 21:811–818.
18. **Olson AL, Zwillich C.** The obesity hypoventilation syndrome. Am J Med 2005; 118:948–956.
19. **Kales A, Bixler EO, Cadieux RJ, et al.** Sleep apnoea in hypertensive population. Lancet 1984; 2:1005–1008.
20. **Ward Flemons W, McNicholas WT.** Clinical predictors of the sleep apnea syndrome. Sleep Med Rev 1997; 1:19–32.
21. **Johns MW.** A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep 1991; 14:540–545.
22. **Netzer NC, Hoegel JJ, Loube D, et al; Sleep in Primary Care International Study Group.** Prevalence of symptoms and risk of sleep apnea in primary care. Chest 2003; 124:1406–1414.
23. **Practice parameters for the indications for polysomnography and related procedures.** Polysomnography Task Force, American Sleep Disorders Association Standards of Practice Committee. Sleep 1997; 20:406–422.
24. Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. The Report of an American Academy of Sleep Medicine Task Force. Sleep 1999; 22:667–689.
25. **Shamsuzzaman AS, Gersh BJ, Somers VK.** Obstructive sleep apnea: implications for cardiac and vascular disease. JAMA 2003; 290:1906–1914.
26. **Chobanian AV, Bakris GL, Black HR, et al; National Heart, Lung, and Blood Institute Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; National High Blood Pressure Education Program Coordinating Committee.** The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. JAMA 2003; 289:2560–2572. Erratum in JAMA 2003; 290:197.
27. **Somers VK, Dyken ME, Clary MP, Abboud FM.** Sympathetic neural mechanisms in obstructive sleep apnea. J Clin Invest 1995; 96:1897–1904.
28. **Morgan BJ, Denahan T, Ebert TJ.** Neurocirculatory consequences of negative intrathoracic pressure vs asphyxia during voluntary apnea. J Appl Physiol 1993; 74:2969–2975.
29. **Kato M, Roberts-Thomson P, Phillips BG, et al.** Impairment of endothelium-dependent vasodilation of resistance vessels in patients with obstructive sleep apnea. Circulation 2000; 102:2607–2610.
30. **Fletcher EC, Lesske J, Culman J, Miller CC, Unger T.** Sympathetic denervation blocks blood pressure elevation in episodic hypoxia. Hypertension 1992; 20:612–619.
31. **Brooks D, Horner RL, Kozar LF, Render-Teixeira CL, Phillipson EA.** Obstructive sleep apnea as a cause of systemic hypertension. Evidence from a canine model. J Clin Invest 1997; 99:106–109.
32. **Peppard PE, Young T, Palta M, Skatrud J.** Prospective study of the association between sleep-disordered breathing and hypertension. N Engl J Med 2000; 342:1378–1384.
33. **Nieto FJ, Young TB, Lind BK, et al.** Association of sleep-disordered breathing, sleep apnea, and hypertension in a large community-based study. Sleep Heart Health Study. JAMA 2000; 283:1829–1836.
34. **Ali NJ, Davies RJ, Fleetham JA, Stradling JR.** The acute effects of continuous positive airway pressure and oxygen administration on blood pressure during obstructive sleep apnea. Chest 1992; 101:1526–1532.
35. **Dimsdale JE, Loredo JS, Profant J.** Effect of continuous positive airway pressure on blood pressure: a placebo trial. Hypertension 2000; 35(1 Pt 1):144–147.
36. **Barbe F, Mayoralas LR, Duran J, et al.** Treatment with continu-

ous positive airway pressure is not effective in patients with sleep apnea but no daytime sleepiness. A randomized, controlled trial. Ann Intern Med 2001; 134:1015–1023.
37. **Robinson GV, Smith DM, Langford BA, Davies RJ, Stradling JR.** Continuous positive airway pressure does not reduce blood pressure in nonsleepy hypertensive OSA patients. Eur Respir J 2006; 27:1229–1235.
38. **Campos-Rodriguez F, Grilo-Reina A, Perez-Ronchel J, et al.** Effect of continuous positive airway pressure on ambulatory BP in patients with sleep apnea and hypertension: a placebo-controlled trial. Chest 2006; 129:1459–1467.
39. **Pepperell JC, Ramdassingh-Dow S, Crosthwaite N, et al.** Ambulatory blood pressure after therapeutic and subtherapeutic nasal continuous positive airway pressure for obstructive sleep apnoea: a randomised parallel trial. Lancet 2002; 359:204–210.
40. **Becker HF, Jerrentrup A, Ploch T, et al.** Effect of nasal continuous positive airway pressure treatment on blood pressure in patients with obstructive sleep apnea. Circulation 2003; 107:68–73.
41. **Alex CG, Onal E, Lopata M.** Upper airway occlusion during sleep in patients with Cheyne-Stokes respiration. Am Rev Respir Dis 1986; 133:42–45.
42. **Tkacova R, Niroumand M, Lorenzi-Filho G, Bradley TD.** Overnight shift from obstructive to central apneas in patients with heart failure: role of PCO2 and circulatory delay. Circulation 2001; 103:238–243.
43. **Sin DD, Fitzgerald F, Parker JD, Newton G, Floras JS, Bradley TD.** Risk factors for central and obstructive sleep apnea in 450 men and women with congestive heart failure. Am J Respir Crit Care Med 1999; 160:1101–1106.
44. **Chan J, Sanderson J, Chan W, et al.** Prevalence of sleep-disordered breathing in diastolic heart failure. Chest 1997; 111:1488–1493.
45. **Shahar E, Whitney CW, Redline S, et al.** Sleep disordered breathing and cardiovascular disease: cross-sectional results of the Sleep Heart Health Study. Am J Respir Crit Care Med 2001; 163:19–25.
46. **Shepard JW Jr, Pevernagie DA, Stanson AW, Daniels BK, Sheedy PF.** Effects of changes in central venous pressure on upper airway size in patients with obstructive sleep apnea. Am J Respir Crit Care Med 1996; 153:250–254.
47. **Mansfield DR, Gollogly NC, Kaye DM, Richardson M, Bergin P, Naughton M.** Controlled trial of continuous positive airway pressure in obstructive sleep apnea and heart failure. Am J Respir Crit Care Med 2004; 169:361–366.
48. **Kaneko Y, Floras JS, Usui K, et al.** Cardiovascular effects of continuous positive airway pressure in patients with heart failure and obstructive sleep apnea. N Engl J Med 2003; 348:1233–1241.
49. **Punjabi NM, Sorkin JD, Katzel LI, Goldberg AP, Schwartz AR, Smith PL.** Sleep-disordered breathing and insulin resistance in middle-aged and overweight men. Am J Respir Crit Care Med 2002; 165:677–682.
50. **Hanly P, Sasson Z, Zuberi N, Lunn K.** ST-segment depression during sleep in obstructive sleep apnea. Am J Cardiol 1993; 71:1341–1345.
51. **Marin JM, Carrizo SJ, Vicente E, Agusti AG.** Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: an observational study. Lancet 2005; 365:1046–1053.
52. **Dyken ME, Somers VK, Yamada T, Ren ZY, Zimmerman MB.** Investigating the relationship between stroke and obstructive sleep apnea. Stroke 1996; 27:401–407.
53. **Mohsenin V.** Sleep-related breathing disorders and risk of stroke. Stroke 2001; 32:1271–1278.
54. **Parra O, Arboix A, Bechich S, et al.** Time course of sleep-related breathing disorders in first-ever stroke or transient ischemic attack. Am J Respir Crit Care Med 2000; 161:375–380.
55. **McArdle N, Riha RL, Vennelle M, et al.** Sleep-disordered breathing as a risk factor for cerebrovascular disease: a case-control study in patients with transient ischemic attacks. Stroke 2003; 34:2916–2921.
56. **Yaggi HK, Concato J, Kernan WN, Lichtman JH, Brass LM, Mohsenin V.** Obstructive sleep apnea as a risk factor for stroke and death. N Engl J Med 2005: 353:2034–2041.
57. **Teran-Santos J, Jimenez-Gomez A, Cordero-Guevara J.** The association between sleep apnea and the risk of traffic accidents. Cooperative Group Burgos-Santander. N Engl J Med 1999; 340:847–851.
58. **Barger LK, Cade BE, Ayas NT, et al; Harvard Work Hours, Health, and Safety Group.** Extended work shifts and the risk of motor vehicle crashes among interns. N Engl J Med 2005; 352:125–134.
59. **Ryan CF.** Sleep x 9: an approach to treatment of obstructive sleep apnoea/hypopnoea syndrome including upper airway surgery. Thorax 2005; 60:595–604.
60. **Kushida CA, Littner MR, Hirshkowitz M, et al; American Academy of Sleep Medicine.** Practice parameters for the use of continuous and bilevel positive airway pressure devices to treat adult patients with sleep-related breathing disorders. Sleep 2006; 29:375–380.
61. **Littner M, Hirshkowitz M, Davila D, et al.** Standards of Practice Committee of the American Academy of Sleep Medicine. Practice parameters for the use of auto-titrating continuous positive airway pressure devices for titrating pressures and treating adult patients with obstructive sleep apnea syndrome. An American Academy of Sleep Medicine report. Sleep 2002; 25:143–147.
62. **Buchwald H, Avidor Y, Braunwald E, et al.** Bariatric surgery: a systematic review and meta-analysis. JAMA 2004; 292:1724–1737.
63. **Puhan MA, Suarez A, Lo Cascio C, Zahn A, Heitz M, Braendli O.** Didgeridoo playing as alternative treatment for obstructive sleep apnoea syndrome: randomised controlled trial. BMJ 2006; 332:266–270.
64. **Janson C, Gislason T, Bengtsson H, et al.** Long-term follow-up of patients with obstructive sleep apnea treated with uvulopalatopharyngoplasty. Arch Otolaryngol Head Neck Surg 1997; 123:257–262.
65. **Garrigue S, Bordier P, Jais P, et al.** Benefit of atrial pacing in sleep apnea syndrome. N Engl J Med 2002; 346:404–412.
66. **Simantirakis EN, Schiza SE, Chrysostomakis SI, et al.** Atrial overdrive pacing for the obstructive sleep apnea-hypopnea syndrome. N Engl J Med 2005; 353:2568–2577.
67. **Sinha AM, Skobel EC, Breithardt OA, et al.** Cardiac resynchronization therapy improves central sleep apnea and Cheyne-Stokes respiration in patients with chronic heart failure. J Am Coll Cardiol 2004:44:68–71.
68. **Gentil B, Lienhart A, Fleury B.** Enhancement of postoperative desaturation in heavy snorers. Anesth Analg 1995; 81:389–392.
69. **Gupta RM, Parvizi J, Hanssen AD, Gay PC.** Postoperative complications in patients with obstructive sleep apnea syndrome undergoing hip or knee replacement: a case-control study. Mayo Clinic Proc 2001; 76:897–905.
70. **Gross JB, Bachenberg KL, Benumof JL, et al; American Society of Anesthesiologists Task Force on Perioperative Management.** Practice guidelines for the perioperative management of patients with obstructive sleep apnea: a report by the American Society of Anesthesiologists Task Force on Perioperative Management of patients with obstructive sleep apnea. Anesthesiology 2006; 104:1081–1093.
71. **Rennotte MT, Baele P, Aubert G, Rodenstein DO.** Nasal continuous positive airway pressure in the perioperative management of patients with obstructive sleep apnea submitted to surgery. Chest 1995; 107:367–374.

ADDRESS: *Silke Krieger, MD, Department of General Internal Medicine, S70, Cleveland Clinic, 9500 Euclid Avenue, Cleveland, OH 44195; e-mail krieges@ccf.org*