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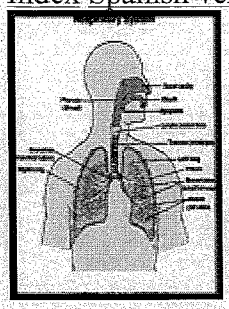


Sleep Apnea

What is sleep apnea?

Sleep apnea is a serious sleep problem. If you have it, you stop breathing for more than 10 seconds at a time many times while you sleep. Another term for this problem is obstructive sleep apnea.

Sleep apnea affects between 2 and 10% of people. It is more common in men than in women. It is also more common in people who are overweight, but there are many people with normal weight who have sleep apnea.

How does it occur?

During normal sleep, throat muscles relax. If, when this happens, there is too little room inside your throat, or too much tissue pressing on the outside of your throat, your airway can become blocked. This blockage stops the movement of air and the amount of oxygen in your blood drops. The drop in oxygen causes the brain to send a signal for you to wake up so that you open up the airway in your throat and start breathing again. If you have sleep apnea, this cycle may repeat as often as 50 or more times an hour. Generally you will not remember waking up but the many arousals will make you sleepy the next day.

Being overweight may cause a narrowing of your airway. Other possible causes of sleep apnea are:

- tobacco smoking
- drinking a lot of alcohol
- lung disease
- an abnormal sleep pattern because of an irregular work schedule or rotating shift work.

Some people inherit a tendency to have sleep apnea.

What are the symptoms?

If you have sleep apnea, your body gets less oxygen when you sleep and you don't sleep well. Common symptoms of sleep apnea are:

- loud snoring interrupted with pauses in breathing, followed by loud gasps
- not feeling rested when you wake up in the morning
- morning headaches

- tiredness or sleepiness during the day
- trouble concentrating
- anxiety, irritability, or depression
- a strong desire to take afternoon naps
- sleepiness while driving.

Many people who snore do not have sleep apnea, but nearly everyone who has sleep apnea snores. If you snore and feel you do not usually get a good night's rest, you should ask your health care provider if you might have sleep apnea.

How is it diagnosed?

Your health care provider may:

- Ask you about your health history and your family's health history.
- Examine you, especially your throat and nasal passages.
- Order blood tests, including a check of the function of your thyroid gland.
- Do a sleep study at a sleep disorders clinic or sleep lab. Your heart rate, brain waves, chest movement, and blood oxygen levels will be measured while you sleep. The study will help determine if the movement of air slows during sleep or if your air movement stops completely during sleep. It will also show how often this happens during sleep.

How is it treated?

It is very important to treat sleep apnea. Untreated sleep apnea can have very serious long-term effects on your health. It may increase your risk of high blood pressure, heart attacks, and sudden death. Effective treatment of sleep apnea may result in normal blood pressure, relief of fatigue, and weight loss.

The most common treatment is use of a machine that sends pressurized air into your nose and throat at night. How much pressure you need is determined by the sleep study. Your health care provider will carefully supervise your use of this breathing machine because minor adjustments may need to be made so it works right for you. This treatment is called continuous positive airway pressure (CPAP).

If you have pressure on your throat because of excess fatty tissue in your throat, your health care provider may suggest a weight-loss program. It may be hard for you to lose weight because you are extremely tired and lack energy to exercise. Use of the breathing machine may help you rest well enough to begin changes in your diet and to increase your physical activity so you can lose weight.

Surgery may be an option if you cannot use the breathing machine regularly and properly. A surgical treatment might include changing the position of the air passage in the nose or removing the tonsils.

Other possible treatments currently being studied are:

- medicines that change the brain chemistry and help muscle tone increase during sleep
- pacemakers that sense when blockages are occurring and stimulate throat muscles to open up the throat before you wake up.

It is too early to say if these experimental treatments will become acceptable treatments of sleep apnea.

How long will the effects last?

If your sleep apnea is caused by a reversible problem, such as overweight or something that can be corrected with surgery, your sleep apnea can be cured. For most people, however, sleep apnea will always be a problem and the CPAP machine will need to be used regularly to get good quality sleep and to prevent the serious

complications of sleep apnea.

How can I take care of myself?

- If you think you may have sleep apnea, see your health care provider.
- If you are being treated for sleep apnea, make sure you go to all your follow-up appointments with your provider. If you lose or gain a lot of weight or have new symptoms, talk to your provider to see if you need to change your treatment.

How can I help prevent sleep apnea?

Proper weight control, exercise (according to your health care provider's recommendations), good sleeping habits, not smoking, and avoiding excessive alcohol use will help you have general good health and may help prevent sleep apnea.

For more information, call or write:

American Academy of Sleep Medicine
Phone: (708) 492-0930
Web site: http://www.aasmnet.org
Professional society representing practitioners of sleep medicine and sleep research

Written by Katherine Dinsdale.
Published by McKesson Provider Technologies.
Last modified: 2005-10-12
Last reviewed: 2005-09-01

Adult Health Advisor 2005.4 Index
Adult Health Advisor 2005.4 Credits

6/12/2003: MEDICAL COMPLICATIONS OF OBSTRUCTIVE SLEEP APNEA

Richard A. Dart, Humberto Vidaillet

Chapter 247. Sleep Apnea

Sleep apnea is defined as an intermittent cessation (10 s to 3 min) of airflow at the nose and mouth during sleep. Frequency of episodes may be from very few to as many as several hundred in one night's sleep. Obstructive sleep apnea (OSA) occurs as the result of occlusion of the oropharyngeal airway, as opposed to a transient cessation of neural stimulation to the respiratory muscles as occurs in central sleep apnea (CSA). The latter will not be specifically discussed in this review, although many of the complications of OSA may also accompany CSA.

Young and colleagues (1997) have found that 2% of all middle-aged females and 4% of all middle-aged males have clinically important sleep apnea. It is estimated that approximately 50% of all middle-aged, obese, hypertensive men have sleep apnea. Approximately 75% of patients with OSA have a body weight >120% of ideal, and OSA prevalence increases with neck circumference. There is a familial predisposition to OSA; heritable craniofacial features that predispose to upper airway occlusion during sleep may run in families.

Traditionally, daytime sleepiness has been considered the most important consequence of sleep apnea. This review, however, will focus on other far more serious potential complications that some evidence suggests may arise as a result of OSA, including cardiac arrhythmias, myocardial infarction, pulmonary hypertension, and stroke. While there are few methodologically rigorous population-based studies at the present time, it is highly suspected that the progression of heart failure may be accelerated as a consequence of adverse hemodynamic and adrenergic loads accompanying OSA.

Pathogenesis

The causes of upper airway obstruction may include nasal septal deviation, hypertrophied turbinates, nasal polyps, midfacial hypoplasia, lymphoidal hyperplasia, macroglossia, neoplasms, retrognathia, micrognathia, retroglossal narrowing, and obesity.

The relationship between sleep apnea and hypertension has long played a role in theories of cardiovascular and/or cerebrovascular risk factors, (Table 1), although a causal relationship has been difficult to prove.

There are four key pathophysiologic features of OSA: (1) an exaggerated negative intrathoracic pressure against the occluded pharynx, (2) hypoxia, (3) hypercarbia or acidosis, and (4) catecholamine surges occurring with arousals from sleep (Figure 1).

Inspiratory efforts during OSA generate exaggerated negative intrathoracic pressure, which leads to both an increase in left ventricular (LV) afterload and a decrease in LV preload, which in turn cause a reduction in stroke volume. This leads to a concomitant hypoxia and sympathetic response. With each apneic episode, oxygen concentration can drop from a normal of 94% to 50% before arousal breaks the episode. Levels below 85% indicate significant apnea. Depending on the strength of the hypoxic stimulus and sympathetic vasoconstrictor response, blood pressure and heart rate can undergo dramatic changes. Heart rate can, and characteristically does, decrease while blood pressure increases toward the end of apneic episodes. With the cessation of the apneic episode, systemic blood pressure and heart rate return toward baseline.

Intermittent hypoxia during OSA may impair cardiac contractility directly or reduce cardiac output indirectly by increasing pulmonary artery pressure. It may also induce a mismatch between the supply and demand of oxygen, provoking myocardial ischemia especially in those with coronary disease. Apnea-induced hypoxia, hypercapnia, and arousal from sleep trigger sympathetic vasoconstrictor outflow that raises systemic blood pressure and heart rate and further increases afterload. These adverse hemodynamic and sympathetic effects are more pronounced in subjects with heart failure. Long-term exposure to elevated sympathetic neural activity can induce hypertrophy and apoptosis of myocytes and predispose patients to cardiac arrhythmias.

Pathophysiologic mechanisms that may cause or contribute to systemic high blood pressure in OSA include hypoxia, catecholamine surges, and hypercarbia. There may also be a role for a cholinergic interaction.

The nightly recurrence of prolonged apneic periods may contribute to cardiac damage. Through this complex of recurring pathophysiologic cycles, there result chronic abnormalities in cardiovascular autonomic regulation during both sleep and wakefulness, which may ultimately result in a general increase in sympathetic nervous activity, decreased baroreflex

sensitivity and heart rate variability, and increased oscillations in blood pressure.

SYSTEMIC HYPERTENSION

Clinically, there is convincing evidence based on rigorous population-based studies in favor of a modest but definite association between OSA and systemic hypertension independent of age, obesity, and other confounding factors (Table 2). However, among patients with OSA of equal severity, some develop hypertension and others do not. Animal experiments suggest that vascular responses to intermittent hypoxia are at least partially under genetic control. Thus, there may be a subset of humans with a genetic predisposition to develop systemic hypertension in response to OSA.

Obesity is a risk factor for both pulmonary and systemic hypertension in patients with OSA. Obesity, restricted ventilatory patterns, and reduced chemosensitivity to hypoventilation may be responsible for daytime hypoxia and pulmonary hypertension in OSA patients.

Pulmonary Hypertension

In the absence of LV dysfunction, daytime hypoxemia, pulmonary thromboembolic disease, vasculitis, or other identifiable causes of pulmonary hypertension, OSA should be considered. In patients with isolated, unexplained pulmonary hypertension who initially present with bilateral leg edema, OSA appears to be common. These patients lack symptoms of heart failure (such as orthopnea, paroxysmal nocturnal dyspnea, and dyspnea on exertion). For patients with bilateral pedal edema, the most cost-effective strategy may be to bypass the echocardiogram and refer the patient to a sleep laboratory. Failure to consider OSA as a possible cause of pulmonary hypertension and failure to order polysomnography (sleep study) might lead physicians to conclude erroneously that a patient's primary diagnosis is pulmonary hypertension, when in fact the correct diagnosis may be pulmonary hypertension secondary to OSA.

Whether OSA causes pulmonary hypertension remains to be proven. If so, the mechanism is likely to be vasoconstrictive as opposed to passive, hyperkinetic, obstructive, or obliterative. Unlike systemic arteries that vasodilate in response to hypoxia or hypoxemia, the pulmonary arteries react by vasoconstriction. Long-standing vasoconstriction can lead to medial hypertrophy and intimal proliferation. It is possible that patients with OSA have increased pulmonary vascular sensitivity to hypoxemia; the pulmonary hypertension might also be related to long-term changes in the vascular architecture related to long-standing nocturnal hypoxemia. If one could demonstrate that effectively treating OSA decreases or normalizes pulmonary artery pressure, one could prove that obstructive sleep apnea causes pulmonary hypertension.

ARRHYTHMIAS

While far more research is needed to elucidate the influence of OSA on arrhythmias, heart rates in patients with OSA may be highly variable, and respiratory sinus arrhythmia (increased heart rate during inspiration) is common. Usually in patients with OSA, the heart rate decreases during apnea and increases abruptly immediately after apnea, resulting in a cyclic bradycardia-tachycardia pattern. The severity of sinus bradycardia in OSA is related to the duration of apnea and the degree of arterial oxygen desaturation. Patients with sleep apnea have a bradycardic response to the Müller maneuver, suggesting that upper airway obstruction may activate parasympathetic receptors at the site of airway collapse. Hypoxia and acidosis accompanying sleep apnea can result in malignant cardiac arrhythmias and nocturnal sudden death. Hypoxia during apnea results in profound peripheral vasoconstriction. Nocturnal palpitations on awakening may be due to increased catecholamines from apneic phases of sleep apnea syndrome.

Tachyarrhythmias and bradyarrhythmias have been reported in more than 75% of patients with sleep apnea syndrome. During the apneic phase, increases in vagal tone cause sinus bradycardia, sinus pauses of 2-13 sec, and atrioventricular conduction delays in 8% of patients. Atrial and ventricular tachyarrhythmias frequently occur during periods of catecholamine surges and hypoxemia at termination of the apnea. Ventricular ectopy during sleep occurs in 55-75% of patients with OSA, especially when oxyhemoglobin saturation falls below 65%.

Peripheral chemoreceptors are stimulated by cardiovascular sympathetic outflow in patients with OSA, even when normoxic and awake. Under normal conditions, the carotid sinus and aortic arch baroreceptors are activated by an increase in blood pressure, which reflexively inhibits sympathetic outflow and increases cardiac vagal outflow, thereby reducing the heart rate.

The nature of the potential association between OSA and atrial fibrillation or sudden cardiac death remains to be determined.

CORONARY ARTERY DISEASE AND CONGESTIVE HEART FAILURE

OSA is a modest independent risk factor for coronary artery disease (CAD) (Table 2). A diseased myocardium is more susceptible to the adverse effects of OSA than is a normal myocardium. It is uncertain whether OSA causes nocturnal myocardial ischemia and angina in the absence of CAD. In patients with CAD, OSA may be an indicator for a poor prognosis (38% mortality vs 9% in those without OSA). However, nocturnal myocardial ischemia is also known to be silent in some patients. The prevalence of OSA among CAD patients with silent nocturnal ischemia is unknown.

Epidemiologic data suggest that OSA can contribute to the development of both systolic and diastolic LV dysfunction and congestive heart failure (CHF) (Table 2). The population-based risk exceeds that for hypertension, stroke, and CAD. CHF may also contribute to the development of OSA. Approximately 50% of patients with heart failure suffer from OSA or CSA. It is not clear, however, whether OSA can lead to LV hypertrophy in humans.

In patients with CHF of unknown etiology, OSA may contribute to the development of LV hypertrophy and dysfunction. Contributing factors include ischemia and reduced contractility due to hypoxia and cardiac myocyte injury or necrosis due to increased catecholamine stimulation. Epidemiologic evidence suggests that OSA can contribute to the development of both systolic and diastolic LV dysfunction. Again, however, there remains a possibility that CHF can itself contribute to the development of OSA.

STROKE AND ATHEROSCLEROSIS

There is evidence that the OSA population is stroke-prone even in the absence of significant carotid arterial disease. However, there is no direct evidence that OSA can precipitate or accelerate atherosclerosis, although OSA is associated with increased platelet aggregability, which is enhanced by the elevated nocturnal catecholamine levels. Additionally, OSA patients are predisposed to clot formation because their hematocrit, fibrinogen levels, and whole-blood viscosity are all elevated (Table 1). The presence of OSA is associated with a clear but modest increase in the prevalence of stroke due to systemic hypertension, increased platelet aggregability, and blood hypercoagulability (Table 2). During the apneic events, there is a significant decline in cerebral blood flow due to the decreased cardiac output. Following stroke, patients with OSA have worse functional outcomes (excessive daytime sleepiness and impaired cognitive function, reaction times, and simulated driving performance) than patients without OSA. Questions remain, however, as to whether the sleep apnea in these patients precedes the stroke or is a consequence of the stroke.

HORMONAL EFFECTS

OSA has no clear effect on the hormones that regulate blood pressure and fluid volume (i.e., renin, aldosterone, and vasopressin). There is an increase in atrial natriuretic peptide (ANP), however, in proportion to the pulmonary artery pressure and negative intrathoracic pressure swings. ANP promotes diuresis, natriuresis, and vasodilation, and the high nocturnal ANP is the likely cause of nocturia, a common feature of OSA.

COGNITIVE EFFECTS

Sleep apnea can adversely influence vigilance, short-term memory, problem-solving skills, and mood. This may translate into an impaired ability to safely operate a motor vehicle or power equipment. In one study, patients with OSA experienced 2.6 more motor vehicle accidents than the general driving population.

Diagnosis

Patients generally present with excessive daytime fatigue and witnessed evidence of loud snoring with intermittent periods of silence terminated by loud resuscitative snorting. The patients may experience restless sleep, morning headaches, decreased intellectual function, and increased irritability; they may awake with a sensation of choking, gasping, or smothering. On physical examination, the patients may be overweight and have large, thick necks, large tonsils, and/or a large tongue.

OSA should be strongly considered in patients with preexisting cardiovascular diseases, including hypertension; in patients with hypertension that is particularly resistant to drug therapy; in patients with poorly explained episodes of congestive heart failure or syncope, with or without a coexisting cardiomyopathy; and in patients with arrhythmias and/or strokes who also are obese, especially those with morbid obesity.

The manifestations of the cardiovascular complications of sleep apnea are protean but the impact of sleep apnea per se seems to be particularly serious. Patients with sleep apnea are at greater risk principally because they so frequently have the common metabolic disorders associated with obesity, including dyslipidemia, hyperglycemia, and frank diabetes mellitus, both insulin- and non-insulin-dependent.

The clinician needs to maintain a high index of suspicion that this disorder may be present and seek to find it. Clinical clues may include a sleep partner who can confirm that the patient snores and witnesses that the patient stops breathing, or indication on the part of the patient that he or she has morning headaches, confusion, or daytime hypersomnolence.

Polysomnography can be used to monitor thoracoabdominal movements. Oximetry is used to monitor oxyhemoglobin saturation. Digital photoplethysmography can monitor blood pressure and heart rate. LV dimensions and LV ejection fractions can be determined by echocardiography. In some cases, brain wave activity and body position are also recorded.

Treatment

In the management of the patient with OSA, benzodiazepines and other ventilatory depressants should be avoided, and the

patient should be advised against the use of alcohol. Both predispose to OSA in that they selectively decrease the activity of the upper airway dilator muscles but do not influence the output of the phrenic nerve and diaphragm function. This leads to an imbalance between the factors that maintain upper airway patency during sleep and those that promote collapse during sleep. Alcohol also increases the duration of apneic episodes by decreasing the arousal response.

Physical, medical, surgical, and mechanical approaches have all been attempted in the treatment of sleep apnea. Physical approaches have included adjustment of position during sleep, and recommendations of diet and exercise. Pharmacologic treatments have included decongestants, nasal steroids, respiratory stimulants, progesterone, cholinergic augmentation, and nicotine. However, none of the adverse nocturnal effects of OSA is remedied by pharmacologic therapy. Beta blockers decrease daytime blood pressure in hypertensive patients with OSA, but not nocturnal blood pressure since they have no effect on OSA itself.

In severe cases, surgical treatment including septoplasty, uvulopalatopharyngoplasty, laser-assisted uvulopalatoplasty, and maxillary, mandibular, or hyoid surgical advancement can be up to 95% successful. However, many times an inability to accurately localize the site of obstruction in a given patient impairs the ability to select the most appropriate procedure to obtain optimal success.

Two mainstays of OSA treatment have emerged. These are weight loss and/or assisted respiration at night through continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BiPAP).

Tracheostomy or CPAP effectively eliminates OSA, nocturnal hypoxia, and arousals from sleep. In fact, CPAP has become the gold standard for the treatment of apneas. Physiologically, CPAP (1) decreases both nocturnal and daytime sympathetic nervous vasoconstrictor activity in association with decreased blood pressure, (2) decreases nocturnal ANP production and urine excretion, and (3) decreases platelet aggregability in association with reductions in overnight catecholamine levels. In the case of pulmonary hypertension, oxygen is an excellent pulmonary vasodilator, so correction of the hypoxia and eliminating occult nocturnal desaturations can be beneficial, if not curative.

Treatment of OSA by CPAP can significantly reduce daytime systolic blood pressure and heart rate, and it improves LV systolic function in patients already receiving optimal medical treatment for both ischemic and nonischemic heart failure. CPAP attenuates apnea-related surges in sympathetic vasoconstrictor tone. By abolishing hypoxic dips, CPAP also augments the myocardial oxygen supply while reducing oxygen demand. The benefits of nocturnal CPAP carry over into wakefulness.

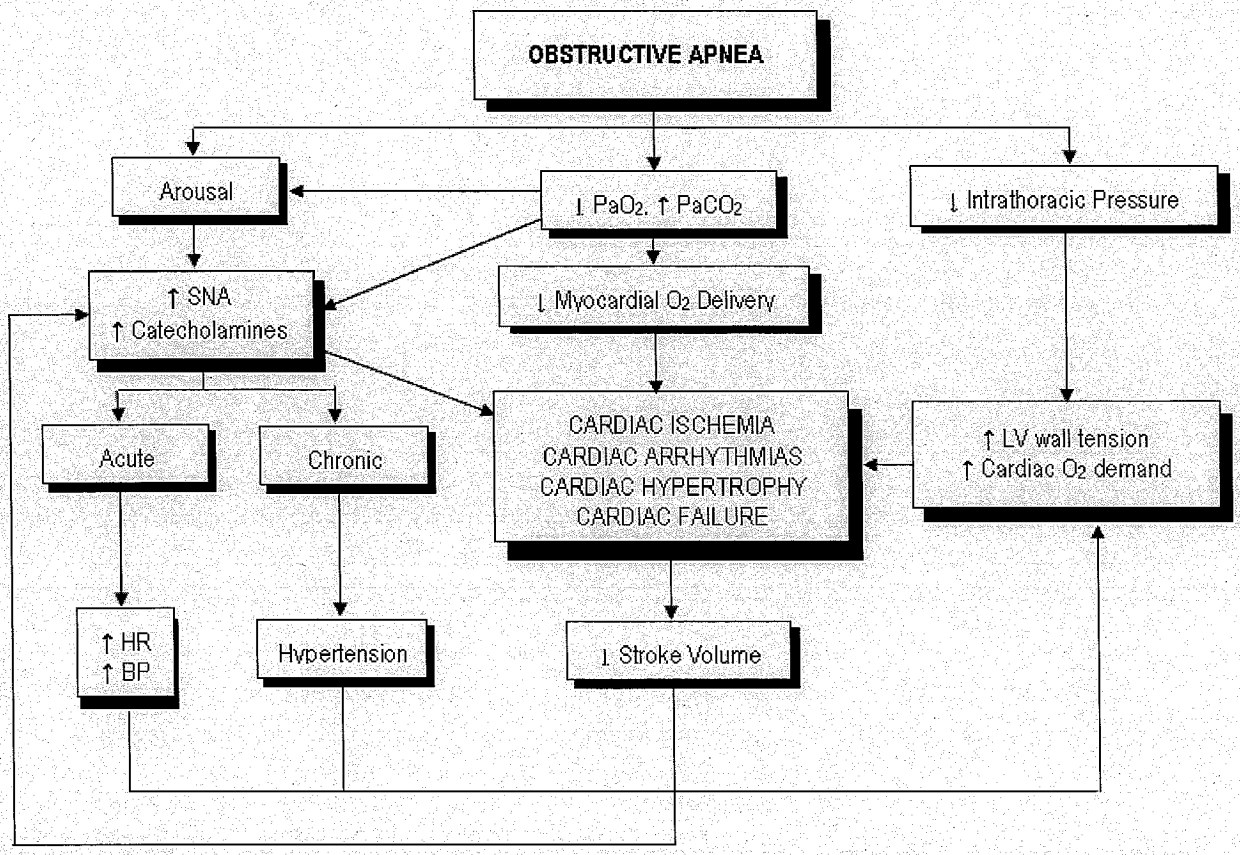
Approximately 25% of patients are unable to tolerate CPAP due to claustrophobia, inability to sleep due to the noise of the machines, and, in some cases, an inability to exhale when the CPAP is in place. For such patients, oral appliances that push the mandible forward or retain the tongue in place, thereby effectively increasing airway size during sleep, have been developed to relieve nocturnal obstructions. These devices successfully treat snoring, 80% of mild to moderate OSA, and 61% of severe OSA. The American Sleep Disorder Association recommends oral appliances for use in patients with primary snoring or mild OSA and in patients with moderate to severe OSA who refuse CPAP or BiPAP. Proper fitting of these appliances is performed by dental practitioners.

Conclusions

The study of cause and effect between OSA and cardiovascular disease is a nascent and emerging field. Only a few methodologically rigorous population-based studies have provided data on associations between OSA and various cardiovascular disorders. When confounding comorbid conditions are removed, the associations are quite modest but remain statistically significant. These associations do not prove causation in one direction or another. The strength of the association and evidence that treatment makes a difference on hard endpoints will have to await further research. Large, randomized trials will be required to determine whether treatment of OSA in patients with systolic and diastolic heart failure improves cardiac function and other cardiovascular outcomes.

Given the current state of knowledge in this area, the presence of sleep apnea should be assessed in patients with preexisting cardiovascular diseases, including hypertension; in patients with hypertension that is particularly resistant to drug therapy; in patients with poorly explained episodes of congestive heart failure or syncope, with or without a coexisting cardiomyopathy; and in patients with arrhythmias and/or strokes who also are obese, especially those with morbid obesity. This is particularly important in the evaluation of patients with symptoms such as fatigue, for these complaints are often attributed to other underlying cardiovascular disease processes (such as heart failure, atrial fibrillation, etc.), when in fact they are often caused or exacerbated by previously undiagnosed OSA. Nasal CPAP is the most effective and widely used intervention for OSA. Even in asymptomatic patients with OSA, while there may be no improvement in subjective well-being, long-term cardiovascular benefits may be expected in the future.

Figure 1



Schematic representation of the pathophysiologic effects of OSA on the cardiovascular system. (After Leung, Bradley, 2001 with permission.)

REFERENCES

BradleyTD, **FlorasJS**: Sleep apnea and heart failure. Part I: Obstructive sleep apnea. Circulation 107:1671, 2003 [PMID: 12668504]

DartRA et al: The association of hypertension and secondary cardiovascular disease with sleep-disordered breathing. Chest 123:244, 2003 [PMID: 12527627]

DartRA et al: Treatment of systemic hypertension in patients with pulmonary disease: COPD and asthma. Chest 123:222, 2003 [PMID: 12527626]

JavaheriS et al: Sleep apnea in 81 ambulatory male patients with stable heart failure: Types and their prevalences, consequences, and presentations. Circulation 97:2154, 1998 [PMID: 9626176]

KanekoY et al: Cardiovascular effects of continuous positive airway pressure in patients with heart failure and obstructive sleep apnea. N Engl J Med 348:1233, 2003 [PMID: 12660387]

LeungRST, **BradleyTD**: Sleep apnea and cardiovascular disease. Am J Respir Crit Care Med 164:2147, 2001 [PMID: 11751180]

PeppardPE et al: Prospective study of the association between sleep-disordered breathing and hypertension. N Engl J Med 342:1378, 2000 [PMID: 10805822]

ShaharE et al: Sleep-disordered breathing and cardiovascular disease: Cross-sectional results of the Sleep Heart Health Study. Am J Respir Crit Care Med 163:19, 2001 [PMID: 11208620]

SinDD et al: Risk factors for central and obstructive sleep apnea in 450 men and women with congestive heart failure. Am J Respir Crit Care Med 160:1101, 1999 [PMID: 10508793]

YoungT et al: Population-based study of sleep-disordered breathing as a risk factor for hypertension. Arch Intern Med 157:1746, 1997 [PMID: 9250236]

Acute Effects

- Reduced myocardial oxygen delivery
  - Intermittent hypoxia
  - Decreased cardiac output
- Increased myocardial oxygen demand
  - Arousal from sleep
  - Sympathetic nervous system activation
  - Increase in left ventricular afterload
    - Negative intrathoracic pressure
    - Increased blood pressure
  - Increased heart rate
- Nocturnal myocardial ischemia
- Nocturnal pulmonary edema
- Cardiac arrhythmias

Chronic Effects

- Autonomic cardiovascular derangements
  - Sympathetic nervous system activation
  - Reduced heart rate variability
  - Impaired baroreflex control of heart rate
  - Systemic hypertension--nocturnal and diurnal
- Myocardial effects
  - Left ventricular hypertrophy
  - Left ventricular dysfunction and failure
- Increased platelet aggregability and blood coagulability
  - Increased susceptibility to thrombotic and embolic cardiac and cerebrovascular events

From Leung, Bradley, 2001, with permission

Cardiovascular Disease	Odds Ratio (95% CI)
Systemic hypertension	1.37 (1.03-1.83)
Congestive heart failure	2.38 (1.22-4.62)
Coronary artery disease	1.27 (0.99-1.62)
Stroke	1.58 (1.02-2.46)