Risk Factors for Obstructive Sleep Apnea in Adults

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OBSTRUCTIVE SLEEP APNEA (OSA) is a sleep disorder characterized by intermittent complete and partial airway collapse, resulting in frequent episodes of apnea and hypopnea.[1] The breathing pauses cause acute adverse effects, including oxyhemoglobin desaturation, fluctuations in blood pressure and heart rate, increased sympathetic activity, cortical arousal, and sleep fragmentation.[1] The condition has received increasing attention during the past 3 decades. Until 1981, the only effective treatment for OSA was tracheostomy.[2] The advent of continuous positive air pressure therapy, an effective noninvasive treatment, was a turning point, and clinical interest began to increase in tandem with the accumulation of research linking OSA to cognitive, behavioral, cardiovascular, and cerebrovascular morbidities (FIGURE).[2,3]

Findings from large population studies in different countries during the last decade have contributed to a better understanding of the epidemiology of OSA.[4-9] In most population studies, OSA status has been indicated by the frequency of apnea and hypopnea events per hour of sleep (apnea-hypopnea index) as determined by polysomnography (a continuous overnight recording of sleep, breathing, and cardiac parameters). The apnea-hypopnea index cutpoints of 5, 15, and 30 (with or without daytime sleepiness) are com-

monly used to indicate mild, moderate, and severe OSA, respectively. These studies have demonstrated that OSA is highly prevalent in adults (TABLE[4-6]). Approximately 1 in 5 adults has at least mild OSA and 1 in 15 adults has OSA of moderate or worse severity.

In the United States, 75% to 80% of OSA cases that could benefit from treatment remain undiagnosed.[10,11] Associations of OSA with serious morbidity have raised concern that untreated OSA is a substantial but underappreciated public health threat. Primary care physicians are currently being encouraged to be alert to OSA symptoms of disruptive snoring, breathing pauses, and excessive daytime sleepiness in their patients.[1,3,12,13] It is important that physicians also recognize that not all OSA patients are "Pickwickian" (ie, male, obese, sleepy, snoring, and middle-aged), a stereotype that emerged from clinical observations of the highly selective patient populations observed in earlier years. The goal of this article is to review recent findings from population-based epidemiology studies on risk factors for OSA in adults.

Demographic Characteristics

Comparison of the male to female ratio in OSA patient populations (8:1) and in undiagnosed OSA from populations studies (2:1) indicate that women with OSA are less likely to be evaluated and diagnosed.[3] Furthermore, some data show poorer survival in female OSA patients, suggesting that OSA in women may be diagnosed late in the course of the disease or may not be aggressively treated.[14] Awareness of OSA prevalence in women has increased, but a greater understanding of sex differences in etiology, presentation, clini-

cal management, and outcomes of OSA is needed.

The prevalence of OSA increases with age, with a 2- to 3-fold higher prevalence in older persons (≥65 years) compared with those in middle age (30-64 years). However, this increase plateaus after 65 years.[4,5,15] It is possible that the observed plateau is due to a relative increase in mortality from OSA after 65 years, but data to address this are sparse. Some data suggest that OSA in older age is a condition distinct from that of middle age. In the Pennsylvania cohort,[4] OSA was less severe in older vs middle-aged persons. That study also addressed central sleep apnea (apnea due to episodic pauses in respiratory effort rather than airway collapse) and found it exclusively in the older age group.[4] Other data suggest that the associations of OSA with hypertension, sleepiness, and cognitive dysfunction are weaker in older vs middle-aged persons.[3] These findings also raise questions regarding case finding and treatment of OSA in older persons. However, methodological issues including cohort effects and measurement error may explain the differences in outcomes by age group. A better understanding of sleep-related breathing disorders in older age and how they differ, if at all, from the typical OSA of middle age is crucial for proper clinical management of older patients with OSA.

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Figure. Risk Factors, Symptoms, Outcomes, and Comorbid Conditions of Obstructive Sleep Apnea (OSA) in Adults
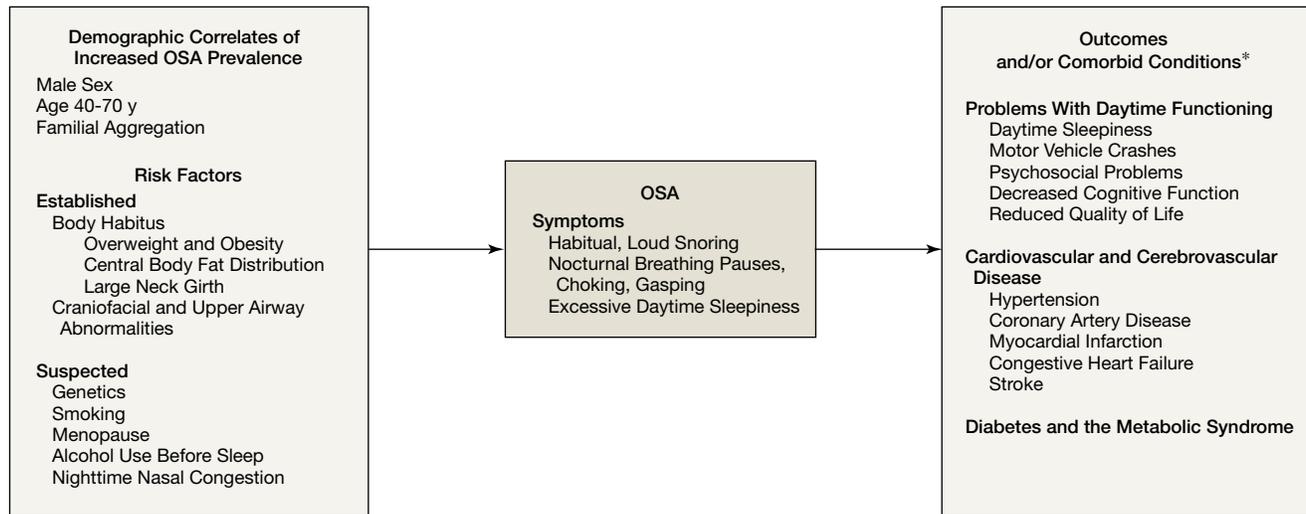
*These conditions are associated with OSA. The associations may be due, in part, to common risk factors; they may also reflect a role of OSA in their etiology.

Table. Prevalence of Obstructive Sleep Apnea (OSA) by Sex and Age Group: 2 US Population Studies[4-6]

Age, y	% (95% Confidence Interval)			
	Mild or Worse OSA*		Moderate or Worse OSA†	
	Women	Men	Women	Men
Wisconsin State Employees (N = 691)[6]				
30-39	6.5 (1.4-11.0)	17.0 (9.6-25.0)	4.4 (1.1-7.3)	6.2 (1.9-10.0)
40-49	8.7 (4.2-13.0)	25.0 (18.0-32.0)	3.7 (1.0-6.5)	11.0 (6.7-16.0)
50-59	16.0 (5.2-26.0)	31.0 (21.0-40.0)	4.0 (0-10.0)	9.1 (5.1-13.0)
Southern Pennsylvania Households (N = 1741)[4,5]				
20-44	‡	7.9 (5.0-12.0)	0.6 (0.2-2.0)	1.7 (0.6-4.4)
45-64	‡	8.7 (4.2-13.0)	2.0 (1.0-4.0)	6.3 (4.2-8.8)
65-100	‡	31.0 (21.0-42.0)	7.0 (4.0-12.0)	13.0 (7.3-23.0)

*All groups with apnea-hypopnea index of 5 or more events/h.
†All groups with an apnea-hypopnea index of 15 or more events/h in the Wisconsin study and all groups with an apnea-hypopnea index of 20 or more events/h in the Pennsylvania study.
‡Not provided.

Risk Factors

Morbid obesity is common in OSA patient populations; however, this extreme is not the case for undiagnosed OSA in the general population. There is a graded increase in OSA prevalence with increasing body mass index (calculated as weight in kilograms divided by the square of height in meters), neck circumference, and waist-to-hip ratio, and OSA may be common in nonobese persons. Obstructive sleep apnea symptoms should not be dismissed simply because the patient does not reflect the "Pickwickian" stereotype.

There is strong evidence that excess weight is a causal factor in OSA but data regarding the feasibility of weight loss as a means of reducing OSA are not conclusive. In a longitudinal analysis of a subset (n=690) of the Wisconsin cohort with a 4-year follow-up,[16] a 10% increase in weight was associated with a 6-fold greater risk of developing OSA among persons initially free of OSA. Similarly, several small studies of surgical or dietary weight loss interventions in clinical populations of patients with OSA who are obese have shown consistent and substantial decreases in OSA severity following weight loss.[3] These latter findings have important clinical implications for overweight patients with OSA who are poor candidates for continuous positive air pressure therapy.

Craniofacial and upper-airway structure have an important role in OSA occurrence[17,18] and may be particularly significant in Asian patients.[19,20] In some subgroups of patients, skeletal or soft tissue abnormalities, including dysmorphisms related to mandibular or maxillary size and position, narrowed nasal cavities, and tonsillar hypertrophy, play an important role in the development of sleep apnea. Enlarged tonsils and adenoids during childhood may cause abnormal growth patterns of the lower face and jaw (adenoidal facies) and predispose to OSA in later life.[21] Surgical correction of these anatomic defects can reduce the apnea-hypopnea index and symptoms of OSA.[21]

Several studies have shown an increased risk of OSA in families of patients with OSA. Although this association may reflect risk factors related to shared lifestyle, there is support for a genetic predisposition to OSA.[22,23] Genetics may explain some possible eth-

nic differences in OSA epidemiology. A higher OSA prevalence was found in a population sample of nonobese Asian patients relative to white patients,[9] and OSA is reported to be more severe in Asian patients.[19] Some studies have reported a higher prevalence of OSA in younger black men and in older black persons but other studies have not found this difference.[15,22]

Smoking is a possible risk factor for OSA but few studies on this topic have been reported. Hypothesized mechanisms for a role of smoking in OSA include airway inflammation and smoking-related disease, as well as effects of declining blood nicotine levels on sleep stability. In the Wisconsin cohort,[24] current smokers were 3 times more likely to have OSA than were former or never smokers. Because there was no increase in OSA for former smokers, it is likely that if smoking does contribute to increased OSA, the effect is reversible with smoking cessation.

Hormonal differences are believed to account for the sex difference in OSA prevalence. Because sex hormone levels dramatically change with menarche, pregnancy, and menopause, it is plausible that these changes modify the risk of OSA. Of the few epidemiology studies that address the effect of female hormonal changes on OSA, most focus on menopause. In an analysis of mid-life women in the population-based Wisconsin Sleep Cohort study,[25] postmenopausal women had 3 times the odds of having moderate or worse OSA compared with premenopausal women, independent of age, body mass index, and other potential confounding factors. The OSA risk increased with duration of menopause up to 5 years postmenopause.[25] In a Pennsylvania population-based cohort of 1000 women, a 4-fold greater risk of OSA was found in postmenopausal women not using hormone therapy vs premenopausal women.[5] These findings support the hormone depletion hypothesis and suggest that hormone therapy may be protective for OSA in postmenopausal women. Findings from the Sleep Heart Health study of 2994 women aged 50 years or older showed hormone therapy users compared with nonusers had half the odds of OSA.[26] However, in a blinded randomized trial involving postmenopausal women, Polo-Kantola et al[27] found only a weak effect of hormone therapy in reducing apnea and hypopnea.

Experimental studies show an acute effect of alcohol on apnea and hypopnea frequency but the effect of long-term alcohol use on the development or progression of OSA is unknown. Findings from epidemiologic studies on self-reported alcohol consumption and OSA have been mixed.[3]

Nasal congestion at night, whether due to allergic rhinitis, acute upper respiratory tract infection, or anatomy, has been linked to snoring and OSA in both experimental and epidemiological studies.[3] A prospective study of OSA in seasonal allergic rhinitis patients indicated that the apnea-hypopnea index increased during the allergen season. In the Wisconsin cohort,[28] the odds ratio for polysomnographically identified OSA with chronic vs no nighttime nasal congestion was 1.8. No studies have addressed the effect of pharmacological treatment of nasal congestion on OSA.

Comorbid Conditions

Obstructive sleep apnea is associated with diabetes, hypertension, coronary artery disease, myocardial infarction, congestive heart failure, and stroke.[1,3,29] The associations may be due in part to risk factors common to all these conditions; they may also reflect a role of OSA in the etiology of these conditions.

The correlates of OSA, including excess body weight and hypertension, overlap with those of diabetes mellitus, and reports that OSA is associated with insulin resistance and other factors related to the metabolic syndrome are increasing.[30] Whether or not there is a mechanistic role of OSA in the metabolic syndrome, it is clear that people with diabetes mellitus should be questioned about OSA symptoms.

Obstructive sleep apnea prevalence is high in patients with hypertension, and a causal role of OSA in hypertension has been suggested by several studies.[1,29,31] In a longitudinal population study,[31] persons with moderate or worse OSA had 3 times the adjusted odds of developing new hypertension compared with persons without OSA. Obstructive sleep apnea is particularly common in patients with resistant hypertension; in a study of patients with hypertension, unsuspected sleep apnea was noted in 83% of those with resistant hypertension, defined as poorly controlled hypertension despite the use of 3 or more antihypertensive agents.[32]

In studies of patients with congestive heart failure, the prevalence of OSA has ranged from 11% to 37%.[33,34] Of major clinical importance is the recent observation that in patients with congestive heart failure, treatment of OSA for 1 month was associated with an increase in ejection fraction and decreases in systolic blood pressure and heart rate.[35] These findings raise the question of whether routine screening for OSA should be performed in patients with congestive heart failure.

Obstructive sleep apnea is also highly prevalent in patients with stroke (43%-72%) and transient ischemic attacks.[36,37] Patients with OSA and stroke have lower functional capacity at admission to a rehabilitation unit and also on discharge.[37] Furthermore, the presence of sleep apnea was shown to be independently related to functional impairment and a 40% longer hospital stay. These findings suggest that treatment of diagnosed OSA might improve the functional outcome and rehabilitation potential in patients with stroke.

Conclusions

This update emphasizes risk factors that will increase the index of suspicion and encourage physicians to embark on a diagnostic path to investigate possible OSA. Although still under investigation, screening questionnaires are available.[13] By increasing the pretest probability, a more efficient use of scarce and expensive diagnostic resources can be achieved. However, case-finding based only on the typical patient characteristics may fail to identify women, older pa-

tients, and mildly obese, or healthy-weight patients with OSA.

Attention to the classic symptoms of disruptive snoring, breathing pauses, and daytime sleepiness is critical but the subjective nature of these conditions creates difficulties in accurate assessment. A patient's awareness of sleep-related breathing problems depends on the adequacy of comments from bedpartners, the difficult quantification of excessive sleepiness, and the perception of daytime dysfunction, which may be masked by adaptation. Furthermore, daytime sleepiness is common for reasons other than OSA, so it is also important to rule out or treat alternative causes including poor sleep hygiene, depression, hypothyroidism, drug abuse, and chronic pain syndromes. If the presence of a treatable condition other than OSA is likely responsible for excessive daytime sleepiness, the decision to refer for polysomnography could be deferred pending treatment of that condition.

Treatment of disruptive snoring or even witnessed apnea without excessive daytime sleepiness is controversial,[12,38] and it is not clear whether the habitual snorer with no additional complaints should be referred to a sleep specialist. Patients with resistant hypertension or cardiovascular conditions, such as congestive heart failure or stroke, who do not manifest the conventional symptoms of sleep apnea, however, may benefit from such a referral. In the absence of clear clinical guidelines for care of an otherwise healthy noncomplaining habitual snorer, a prudent response would be to alert the patient to the health consequences of OSA, the possibility of developing OSA, the importance of excess body weight in the progression of OSA, and the role that smoking, alcohol, and nighttime nasal congestion may play in OSA.

Currently, OSA is underdiagnosed. Physicians should follow a step-by-step approach to come to a clinical judgment for polysomnography in an individual patient. First, consider the possibility of OSA in patients reporting loud, disruptive snoring, witnessed apnea episodes, or excessive daytime sleepiness.

Then, based on more in-depth history and clinical assessment of the updated risk factors described herein, decide whether there is a strong possibility of OSA and need for further evaluation with polysomnography. Third, before referring for polysomnography, consider alternative diagnoses that might account for the patient's symptoms. Finally, have a higher index of suspicion in patients with comorbidities such as congestive heart failure, stroke, and refractory hypertension who are at increased risk for OSA but who may lack conventional symptoms associated with OSA.

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