Pulmonary Impairments Workshop:

Obstructive Sleep Apnea

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Obstructive Sleep Apnea

Introduction

Obstructive sleep apnea (OSA) is a common respiratory impairment that is present in approximately 25% of adults in the US, although prevalence varies by age, sex, body mass index (BMI), race, and ethnicity.

The prevalence of OSA is increasing as obesity becomes more widespread. Not only is there is a high prevalence of OSA in patients with chronic diseases such as resistant hypertension, atrial fibrillation, type 2 diabetes, heart failure, and stroke, but it may also exacerbate these conditions. The risk of death increases significantly if sleep apnea is untreated.

OSA is underdiagnosed and often incompletely treated, in part because the treatment is not well tolerated by patients.

For symptomatic patients, the treatment of OSA has been shown to improve quality of life, improve work performance, lower the rates of motor vehicle accidents, and reduce the risk of chronic health consequences of untreated OSA. Treatment does not reduce the risk of cardiovascular disease, stroke, or metabolic abnormalities in asymptomatic patients.

The life insurance medical director needs to assess and stratify the mortality risk of applicants who have symptoms, such as snoring and excessive daytime sleepiness, as well as those with a confirmed diagnosis of OSA who may or may not be successfully treated.

Definition, Symptoms, and Testing (See Gottlieb & Punjabi *JAMA* 2020 and UpToDate articles)

Obstructive sleep apnea is defined as reduced (hypopnea) or absent (apnea) airflow due to partial or complete collapse of the upper airway during sleep. The impaired airflow should persist for at least 10 seconds and be associated with either cortical arousal or a fall in blood oxygen saturation.

Obstructive apneas and hypopneas cause intermittent hypoxemia and arousal from sleep enough to cause sleep fragmentation, even though the patient may not awaken. The sleep fragmentation results in excessive daytime sleepiness, and the intermittent hypoxemia elevates blood pressure through stimulation of the sympathetic nervous system. Animal models suggest increased catecholamine levels influence insulin sensitivity, and hypoxemic events contribute to inflammation and vascular disease. Significant intrathoracic pressure swings may adversely increase cardiac preload and afterload.

OSA can be diagnosed with either at-home testing or testing in a sleep laboratory. The apnea-hypopnea index (AHI) is typically used to quantify the presence and severity of OSA. The AHI is defined as the number of apneas plus hypopneas per hour of sleep. (The definition of a hypopnea varies, and a common conservative definition requires a 4% drop in blood oxygen saturation.)

Severity of OSA is often graded according to the AHI, although treatment decisions should consider symptoms and comorbid illnesses along with AHI severity:

AHI	Severity
0 to 4.9 events/hr	Normal (No OSA)
5.0 to 14.9 events/hr	Mild
15 to 29.9 events/hr	Moderate
30 or more events/hr	Severe

The most common symptoms of OSA are unrefreshing sleep with excessive sleepiness. Accompanying fatigue is often described as tiredness or lack of energy. While only a minority of patients may report awakening with gasping or choking, this is a highly specific symptom. Snoring is a common, but less specific, symptom.

Questionnaires available for assessing OSA risk include the Berlin Questionnaire, the STOP-Bang Questionnaire, and the Epworth Sleepiness Scale.

Questionnaire	Sensitivity, %	Specificity, %
Berlin Questionnaire	77	44
STOP-Bang Questionnaire	90	36
Epworth Sleepiness Scale	47	62

(Adapted from Gottlieb & Punjabi *JAMA* 2020)

Because of the absence of clear treatment benefit in people without symptoms, the US Preventative Services Task Force does not recommend screening for OSA in people without symptoms. Screening may be appropriate in individuals whose occupation involves driving or in patients with resistant hypertension. Clinicians may consider testing individuals with unexplained nocturia, nocturnal gastroesophageal reflux, morning headache, or frequent nocturnal awakenings, especially in the setting of snoring, witnessed apneas, or obesity.

If OSA is confirmed by a home test, positive airway pressure (PAP) therapy can usually be initiated at home using an automatic titrating PAP device. If there is a high suspicion for OSA and the home test findings are negative for OSA, laboratory-based polysomnography is recommended.

Treatment of OSA

Positive airway pressure (PAP) is the primary therapy for individuals with symptomatic OSA of any severity. The pressure acts as a splint to prevent airway collapse during inspiration. Automatic titrating PAP devices are very effective for many patients; they monitor airflow and adjust pressure in response to changes in flow. Automatic titration may not be appropriate for individuals in whom central sleep apnea is common (e.g. individuals with chronic heart failure). Benefit depends on adherence to therapy, with more hours of use per night associated with greater symptom improvement and greater blood pressure reduction. The Centers for Medicare and Medicaid Services defines adherence as at least 4 hours per night for at least 5 nights a week, but optimal response is achieved with more than 6 hours per night. Newer PAP devices allow for remote monitoring of adherence.

Behavioral measures and medical devices other than PAP can be effective in reducing AHI. For individuals who cannot tolerate PAP therapy, mandibular advancement devices, weight loss, exercise, avoiding sleep in the supine position, and abstaining from alcohol can be beneficial. A follow-up sleep test is needed to determine the magnitude of the AHI reduction.

Treatment with either PAP or oral appliances is not curative. Life-long treatment is typically needed in the absence of weight loss sufficient enough to cause disease remission.

Surgical treatments for OSA modify upper airway soft tissue. Uvulopalatopharyngoplasty (UPPP) involves resection of the uvula and part of the soft palate. Other procedures include tongue reduction, lateral wall pharyngoplasty, or modification of the bony structures of the face, such as maxillomandibular advancement. As with other treatments of OSA, a follow-up sleep test is advised to determine the magnitude of the AHI reduction.

Hypoglossal nerve stimulation (e.g., the Inspire device) requires placement of an electrode to enhance tongue protrusion during sleep. A pressure sensor is placed between the internal and external intercostal muscles to detect inspiratory effort and thus, allowing the hypoglossal nerve stimulation to be coordinated with respiratory effort. Studies show it is effective and well tolerated in approximately two-thirds of those who have failed or declined PAP therapy, recognizing that appropriate patient selection is essential.

There are no medications currently approved for the management of OSA, although wake-promoting medications such as modafinil are approved to manage residual sleepiness after other causes of excessive sleepiness have been excluded.

The benefit of treating individuals with asymptomatic OSA is unclear. The Sleep Apnea Cardiovascular Endpoints (SAVE) Study and the Impact of Sleep Apnea Syndrome in the Evolution of Acute Coronary Syndrome (ISAACC) Study are randomized clinical studies that showed no effect of PAP on reducing rates of myocardial infarction, stroke, or mortality in asymptomatic individuals with OSA. However, cluster analysis (see below) may indicate benefit in select populations.

Treatment-Emergent Central Sleep Apnea (See Chowdhuri and Parthasarathy in UpToDate)

The life insurance medical director may be consulted to opine upon treatment-emergent central sleep apnea (CSA). Careful evaluation of the sleep study report and subsequent follow-up office notes will help guide the mortality assessment.

Treatment-emergent central sleep apnea is the persistence or emergence of central apneas and hypopneas during the titration of PAP therapy without a backup respiratory rate for OSA. It is an incidental polysomnographic finding during the initial in-laboratory titration of CPAP (continuous positive airway pressure) or BiPAP (bilevel positive airway pressure). Patients are usually asymptomatic, although they may sometimes have symptoms of disturbed sleep.

In those individuals confirmed to have OSA (AHI of 5/hr or greater, with predominantly obstructive events) exposed to positive airway pressure without a backup rate, the diagnostic criteria for treatment-emergent CSA include:

- significant resolution of obstructive events, and
- central hypopnea index =>5 events/hr, and
- central apneas and hypopneas make up =>50% of the total number of apneas and hypopneas, and
- symptoms of daytime sleepiness or disrupted sleep.

Treatment-emergent CSA resolves spontaneously in approximately two-thirds of patients on continued CPAP. This should be documented by repeat polysomnography or home sleep apnea testing in 2-3 months to determine if the central apneas have resolved. Persistent central apneas may require a different mode of ventilation.

<u>Prognosis of OSA: More than AHI?</u> (See Zinchuk and Yaggi)

It has long been recognized that the overall AHI does not capture the diversity of the polysomnographic presentations of OSA. To better define specific diagnostic and treatment strategies which may lead to improved patient outcomes, researchers have sought to classify OSA patients into relevant subgroups based upon a variety of OSA characteristics. These characteristics may include signs, symptoms, demographics, polysomnographic and physiologic metrics, or comorbidities. These subgroups are sometimes referred to as phenotypes, and the analytic technique used to perform these studies is called cluster analysis.

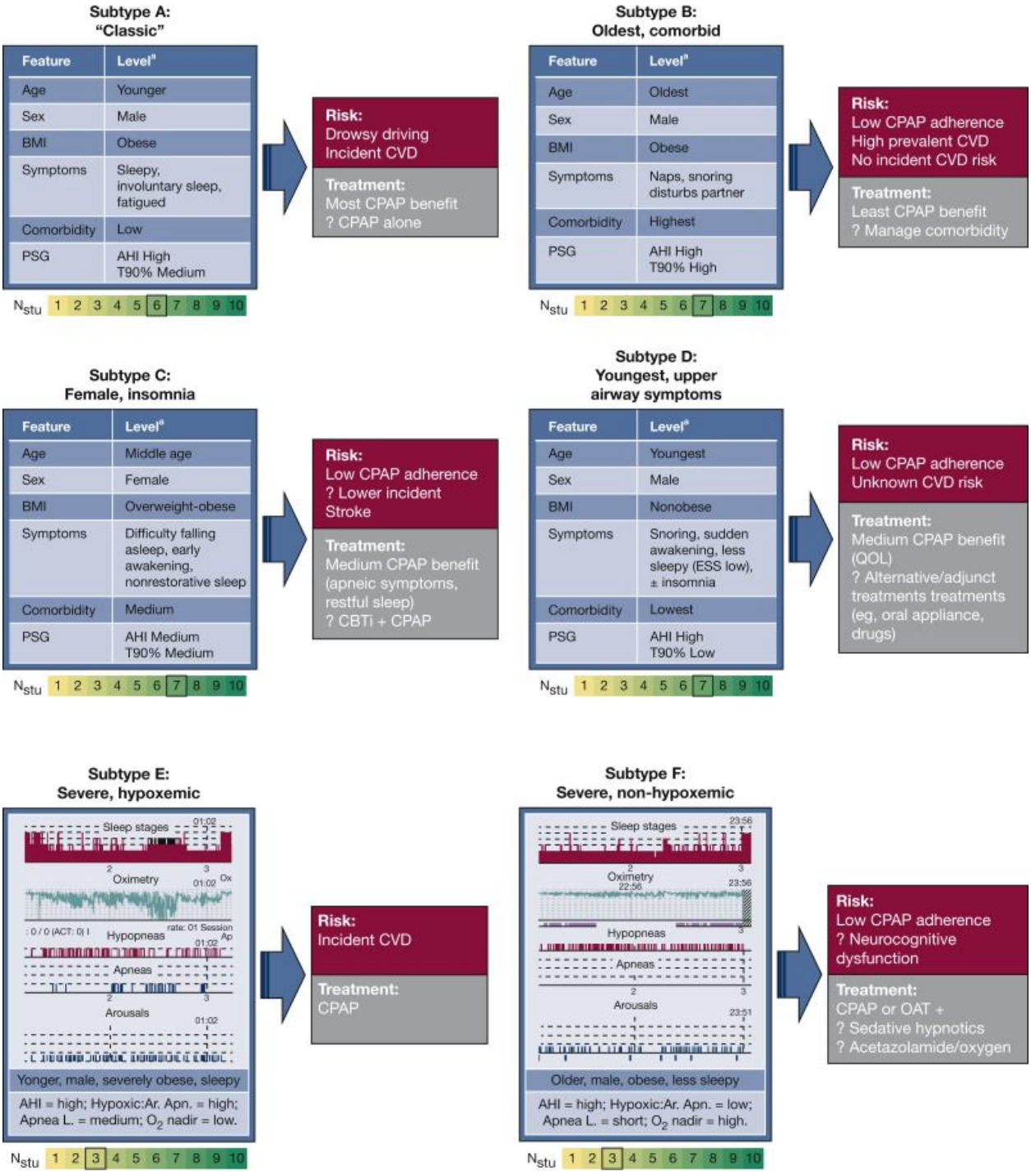
In their 2020 review in *Chest*, Zinchuk and Yaggi anticipate that these "phenotypes may therefore also be used to design more successful clinical trials of CPAP therapy by targeting subtypes of OSA with the highest risk of adverse health outcomes and largest symptomatic benefit of CPAP, such as the excessively sleepy, a group excluded from previous trials of CPAP therapy in CVD."

As shown below, Zinchuk and Yaggi propose 6 potential subtypes of OSA based upon their cluster analysis. Subtypes A through D focus on clusters related to age, BMI, sex, symptoms and comorbidities. Subtypes E and F focus on OSA physiology as assessed by using polysomnography.

For the life insurance medical director, the subtypes remind us to use a holistic evaluation of the applicant's mortality risk by looking beyond the AHI. Comorbidities such as coronary artery disease may present a greater mortality risk than the OSA, especially if hypoxemia is not present.

(I wish to acknowledge and thank Dr. Rod Richie and Dr. Ann M Romaker. Dr. Richie shared with me Dr. Romaker's presentation from the Midwestern Medical Directors Association annual meeting in May, 2022 entitled, "Is OSA What We Think it is? Updates in 2022". Dr. Romaker discussed the phenotypes at length.)

OSA Subtypes (From Zinchuk and Yaggi, *Chest* 2020)



(Nstu is the number of studies that identified analogous clusters.)

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UpToDate: Excellent articles about OSA. Subscription required.

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