

Guidelines for Diagnosis and Treatment of Sleep-related Breathing Disorders in Adults and Children

Definition and classification of sleep related breathing disorders in adults.

Different types and indications for sleep studies (Part 1)

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Guidelines on diagnosis and treatment of sleep-related breathing disorders in adults and children were introduced by the Hellenic Society of Sleep Disorders Working Group in an attempt to fill a major gap in current medical practice in Greece. They consist of the theoretical ground followed by practice recommendations regarding the diagnostic and therapeutic procedures that are currently accepted for the individual management of adults and children.

The guidelines are divided into three parts. The first part entitled "Definition and classification of sleep-related breathing disorders in adults. Different types and indications for sleep studies" refer to different syndromes related to breathing disorders during sleep such as: Central Apnea Syndromes, Cheyne-Stokes Respiration, Obstructive Sleep Apnea Syndrome, Upper Airway Resistance Syndrome, and Alveolar Hypoventilation Syndrome. In addition, major types of sleep studies such as: Full polysomnography, limited sleep study, attended sleep study, unattended sleep study, split-night study were mentioned, along with their indications for diagnostic and therapeutic purposes.

The second part entitled "Treatment of Obstructive Sleep Apnea Syndrome (OSAS) in adults" refers to different types of treatment for OSAS in adults such as Positive Airway Pressure application, oral appliances and surgical treatment. Different types of Positive Airway Pressure devices were presented, along with benefits related to their application. Finally, the issue of compliance to CPAP use is being addressed in this chapter.

The third part entitled "OSAS in children: Diagnosis and treatment" refers to Obstructive Sleep Apnea Syndrome in children. Clinical features, pathogenesis, diagnosis and treatment are also mentioned.

The events leading to the formation of these guidelines are the following: First, a meeting in Athens (February 2008), where topics and committees were selected; later on a consult in Patras (June 2008), where texts were distributed among members and the final acceptance took

place in Alexandroupolis (November 2008).

The whole process and the final presentation were under supervision and acceptance of the Executive Committee of HSSD.

A. Classification of sleep - Related breathing disorders in adults

The first organized effort for the classification of sleep disorders was published in Sleep in 1999 under the title "Diagnostic Classification of Sleep and Arousal Disorders". This classification was further improved and revised with the collaboration of major international sleep societies. The most recent classification was published in 2005 and was entitled "International Classification of Sleep Disorders: Diagnostic and Coding Manual (ICSD-2)"¹. It aimed at introducing a common terminology to everyone related to the field of sleep medicine, thereby improving communication and promoting clinical practice as well as research.

According to the current classification, there are four major types of sleep-related breathing disorders.

1. Central apnea syndromes

- 1.1. Primary central apnea
- 1.2. Cheyne - Stokes respiration
- 1.3. Periodic respiration of high altitude
- 1.4. Central apneas without Cheyne-Stokes respiration secondary to other disorders (vascular, malignant, degenerative or traumatic disorders of the central nervous system, cardiac/renal disorders)
- 1.5. Central apneas caused by medicine or other substances
- 1.6. Primary sleep apnea of newborn

2. Obstructive apnea syndromes

- 2.1. Obstructive apnea in adults
- 2.2. Obstructive apnea in children

3. Hypoventilation/ hypoxemia syndromes associated with sleep

- 3.1. Non-obstructive alveolar hypoventilation, idiopathic
- 3.2. Congenital central hypoventilation
- 3.3. Hypoventilation/hypoxemia secondary to other disorders: lung parenchymal, airway (e.g. COPD), or vascular (e.g. pulmonary hypertension) disorders; neuromuscular disorders; thoracic wall abnormalities; obesity.

4. Undefined/non-specific sleep disorders

Disorders without specific characteristics to allow their classification in any of the previous categories. Further investigation is required.

B. Events/indexes of sleep - Related breathing disorders and arousals¹⁻³

Definitions

Apnea is defined as:

- 1. Reduction in airflow greater than $\geq 90\%$ of baseline*, recorded by oronasal thermistors or nasal pressure cannulas.
- 2. Duration ≥ 10 sec.
- 3. Aforementioned reduction in airflow at least 90% of the event.

Classification of apneas based on respiratory effort:

- 1. Obstructive apnea: respiratory effort is recorded throughout the event.
- 2. Central apnea: absence of respiratory effort throughout the event.
- 3. Mixed apnea: there is absence of respiratory effort at the beginning of the event followed by increasing respiratory effort during the second half.

Hypopnea is defined as:

- 1. Reduction in airflow $\geq 30\%$ from baseline¹, recorded by nasal pressure cannulas or alternatively by induction plethysmography or oronasal thermistors.
- 2. Duration ≥ 10 sec.
- 3. Aforementioned reduction in airflow at least 90% of the event.
- 4. Reduction in saturation at least $\geq 4\%$ from baseline SpO₂% prior to the event.

Alternatively: Hypopnea can be defined as a respiratory event that meets the following criteria:

- 1. Reduction in airflow $\geq 50\%$ from baseline, recorded by nasal pressure cannulas or alternatively by induction plethysmography or oronasal thermistors.
- 2. Duration ≥ 10 sec.
- 3. Aforementioned reduction in airflow at least 90% of the event.

- 4. Reduction in saturation $\geq 3\%$ from baseline prior to the event or appearance of an arousal.

Respiratory effort- related arousal (RERA)

It is a breathing disorder characterized by obstructive upper airway airflow reduction (which does not meet the criteria of apnea or hypopnea), associated with increased respiratory effort that resolves with the appearance of arousals (RERAs). It is preferably recorded with esophageal manometry, although nasal manometry or induction plethysmography is also appropriate. Diagnostic criteria are:

- 1. A series of respiratory cycles of increasing/ decreasing effort or flattening, recorded by nasal manometry and leading to an arousal that cannot be defined as apnea or hypopnea.
- 2. Duration ≥ 10 sec.

Cheyne-Stokes respiration is established by recording at least three crescendo-decrescendo fluctuations in respiration, as well as one of the following:

- 1. Five or more central apneas or hypopneas per hour of sleep.
- 2. Duration of crescendo-decrescendo fluctuations in respiration at least 10 continuous minutes.

Hypoventilation: It is defined as an increase of PaCO₂ levels ≥ 10 mm Hg during sleep compared to PaCO₂ levels in wakefulness or in supine position.

Persistent hypoxemia cannot sufficiently establish the diagnosis of hypoventilation.

Increased levels of PaCO₂ in a blood sample taken immediately after arousal is suggestive of hypoventilation.

Note: Precise measurement of minimum duration of hypoventilation and of PaCO₂ levels with alternative methods is currently unavailable. Recordings of end expiratory CO₂ as well as transdermal PaCO₂ have proved to be reliable in clinical practice and can also be used.

Apnea-Hypopnea index (AHI): The number of apneas and hypopneas per hour of sleep, confirmed by electroencephalogram (EEG).

Respiratory Disturbance Index (RDI): The number of apneas, hypopneas and RERAs per hour of sleep, confirmed by EEG.

Note: Both indexes of sleep-related breathing disorders can be used in full polysomnography. In limited sleep studies (which does not include EEG), RDI is defined as the number of apneas and hypopneas per hour of sleep recorded.

Arousal: It is defined as a sudden change of EEG fre-

1: Baseline is considered the moderate of steady respiration and ventilation during the last 2 minutes prior to the event for patients with fixed respiration pattern, or the moderate of the 3 longest respirations during the last 2 minutes prior to the event for patients with variable respiration pattern.

*1: Differential diagnosis and classification of hypopneas as obstructive, central or mixed requires measurement of respiratory effort. This is achieved by esophageal manometry or by calibrated induction plethysmography or by diaphragmatic/ intercostal electromyogram. It is suggested that the first definition is used; however in every polysomnographic study it should be stated which definition was used.

quency consisting of alpha and theta activity or waveforms with frequency greater than 16 Hz (but not sleep spindles) and duration 3-15 sec. Normal sleep is recorded for at least 10 seconds before and after the event. An arousal is not considered wakefulness in the sense that the patient is unconscious of the event.

C. Major clinical syndromes^{1,3}

Primary Central Apnea: It is a rare disorder of unknown cause. It is more prevalent in the middle-aged and elderly; and in male patients. It is attributed to increased sensitivity of chemoreceptors in PaCO_2 leading to derangements in ventilation control. Events of central apnea usually occur in NREM stages 1 and 2 (the duration of which is longer than that of stages S3 and S4) and rarely during REM sleep. The events of central apnea result in disturbance of normal sleep architecture and appearance of nocturnal arousals, daytime sleepiness or insomnia. Blood gas analysis in wakefulness reveals normal or decreased levels of PaCO_2 ($< 40 \text{ mm Hg}$).

Diagnostic criteria: A plus B plus C

- A. Patient reports at least one of the following: daytime sleepiness, frequent arousals or insomnia, arousals with dyspnea.
- B. Polysomnography reveals ≥ 5 central apneas per hour of sleep.
- C. The disorder cannot be attributed to other conditions, use of medicine or substances.

Cheyne-Stokes respiration: It is characterized by repeated episodes of central apneas and hypopneas alternating with prolonged periods of hyperpnea in a crescendo-decrescendo pattern. Symptoms are sleepiness or insomnia and arousals with or without dyspnea. The predisposing factors are: congestive heart failure, cerebrovascular diseases and renal failure.

Diagnostic criteria: A plus B plus C

- A. Polysomnography reveals at least 3 consecutive cycles of crescendo-decrescendo fluctuations in breathing amplitude, combined with at least one of the following criteria:
 - a. Five or more central apneas or hypopneas per hour of sleep.
 - b. Duration of crescendo-decrescendo fluctuations is at least 10 consecutive minutes.
- The pattern of Cheyne-Stokes respiration varies in duration and usually lasts about 60 seconds.
- B. Severe comorbidities, such as congestive heart failure, cerebrovascular diseases and renal failure.
- C. The disorder cannot be attributed to other conditions, use of medicines or other substances.

Obstructive sleep apnea syndrome (OSAS): It is defined as repeated episodes of obstructive apneas and hypopneas during sleep, frequently followed by transient hemoglobin desaturation (hypoxemia) and unconscious (EEG) arousals.

Snoring, episodes of dyspnea, asphyxia or suffocation and body movements are common between apnoeic events; and can cause sleep fragmentation. Feeling of unrefreshing sleep, exhaustion and daytime sleepiness (which is the most common symptom) can severely impair quality of life of the patients. OSAS is considered as an independent risk factor for development of systemic arterial hypertension and cardiovascular events. Its prevalence, using the most rigid diagnostic criteria, is estimated to be 4% and 2% in middle-aged men and women respectively.

Predisposing factors are obesity, congenital or acquired craniofacial and neck defects, menopause, endocrine abnormalities, whereas smoking and alcohol use can precipitate the disorder.

Diagnostic criteria: A, B plus D or C plus D

- A. At least one of the following:
 - 1. Sleepiness, hypersomnolence, exhaustion or insomnia.
 - 2. Arousals with feeling of asphyxiation/suffocation.
 - 3. Snoring, breathing pauses witnessed by sleep partner.
- B. Polysomnography findings:
 - 1. Apnea, hypopnea or RERAs ≥ 5 per hour of sleep.
 - 2. Recording of respiratory effort during part or the whole event.
- C. Polysomnography findings:
 - 1. Apnea, hypopnea or RERAs ≥ 15 per hour of sleep.
 - 2. Recording of respiratory effort during part or the whole event.
- D. The disorder cannot be attributed to other conditions, use of medicines or other substances.

Severity criteria: The criteria of the severity of OSAS are a combination of the severity of daytime sleepiness and the value of apnea-hypopnea index (AHI).

- Severity assessment of daytime sleepiness can be subjective and objective. Subjective assessment is obtained with questionnaires. Epworth Sleepiness Scale (ESS) is the most commonly used, which has a range of 0-24 and a minimum normal value of 10.
- Apnea - Hypopnea Index (AHI) or Respiratory Disturbance Index (RDI)
 - 1.1. Mild: 5-15 events per hour.
 - 1.2. Moderate: 15-30 events per hour.
 - 1.3. Severe: more than 30 events per hour.

Upper Airway Resistance Syndrome (UARS): It is a clinical term diagnostic of patients with RERAs and symptoms of OSAS. RERAs are similar to true obstructive apneas and hypopneas in terms of the pathophysiology and their complications. Therefore, UARS is not considered as an independent disorder rather than one aspect of the spectrum of obstructive sleep disorders and should be diagnosed and treated in this context.

Alveolar Sleep Hypoventilation/Hypoxemia Syndrome (secondary)

It is characterized by hypercapnia and prolonged-persistent hypoxemia during sleep. The haemoglobin desaturation is characterized by lack of saw-tooth pattern or concomitant events of apnea-hypopnea or inspiration flow reduction or snoring.

Patients with significant haemoglobin desaturation, inability to preserve sufficient alveolar ventilation with normocapnia; and generally those who exhibit greater breathing difficulty during diagnostic evaluation in wakefulness are considered to be at greater risk of developing or aggravating hypoventilation/hypoxemia during sleep. Regardless of its etiology, sleep hypoventilation/hypoxemia syndrome is associated with high risk of complications (mostly due to nocturnal hypoxemia), such as: pulmonary hypertension, cardiac arrhythmias, polycythemia, behavioral and cognitive disorders.

Patients with severe respiratory failure of any cause usually will not benefit from a full-night polysomnography; rather than from the successful management of a sleep related disorder. Therefore, any safe and efficacious diagnostic or therapeutic procedure should be considered as a first choice of management.

Diagnostic criteria: A plus B plus C

A. Presence of one of the following disorders:

A1. Chronic Obstructive Pulmonary Disease (COPD) with $\text{FEV}_1/\text{FVC} < 70\%$ of predicted.

A2. Neuromuscular disorder or chest wall abnormality or obesity (pathologic “ventilation pump”).

A3. Parenchymal (e.g. diffuse interstitial lung disease) or vascular disorder (e.g. pulmonary hypertension) of the lung.

B. Presence of one of the following findings in polysomnography or arterial blood gas analysis during sleep:

B1. SpO_2 during sleep $< 90\%$ for > 5 min with minimum value at least 85% ($\text{SpO}_2 \text{ min} \leq 85\%$).

B2. $\text{SpO}_2 < 90\%$ for more than 30% of total sleep duration.

B3. $\text{PaCO}_2 > 45$ mm Hg during sleep or disproportionately increased PaCO_2 levels compared to wakefulness.

C. The disorder cannot be attributed to other conditions, use of medicine or other substances.

D. Types of sleep study³⁻⁸

1. Full night polysomnography

It consists of simultaneous recordings of multiple physiological parameters that distinguish between sleep stages and architecture as well as cardiopulmonary function. It comprises of at least: electroencephalogram (EEG) with two derivations (C3A2, C4A1); electrooculogram (EOC) with 2 derivations; chin electromyogram (EMG); anterior tibialis muscle EMG; oronasal manometry (also described in definitions); chest and abdominal wall movements; hemoglobin saturation; snoring recordings; body position and video monitoring during sleep. It requires a highly equipped laboratory that meets standard qualifications and it is considered as the gold standard for the diagnosis and of the therapeutic application of CPAP or BPAP.

2. Limited studies^{10,11}

They are concomitant and consistent recordings of at least cardiopulmonary parameters. These studies do not allow the estimation and the neurophysiological staging of total sleep duration. An attended limited sleep study is a useful diagnostic tool only when performed by specialized health care providers and under well-defined conditions; otherwise it can be useless or even dangerous to the patient. Necessary requirements for its diagnostic and therapeutic use are:

1. It must be performed exclusively in a qualified sleep centre.

2. It is indicated in patients with moderate or high possibility of OSAS, especially when it is associated with hypersomnolence or major risk factors for cardiovascular complications.

3. Its necessity as a diagnostic tool should be evaluated by a qualified physician and it should be avoided if a full polysomnography or another diagnostic method is indicated, for example in central apnea syndrome, periodic limb movement syndrome, REM behavioural disorder, narcolepsy, etc.

4. The recording appliance must have the option of processing the results.

5. During evaluation of the results, the respiratory events must be scored with the same criteria as in the full polysomnography.

6. Data must be evaluated and interpreted by a highly specialized physician.

7. Given the high rate of falsely negative results (17%), a full polysomnography must be performed when there is strong suspicion of OSAS that cannot be established in a limited sleep study.

8. It can be used for monitoring of OSAS patients under treatment with CPAP or oral appliance or in patients who underwent upper airway surgery; provided that there has been improvement in their clinical presentation and regression of symptoms.

9. The recording appliance must have a minimum of technical specifications listed below.

Technical specifications

The equipment used in a limited sleep study should meet the following specifications, ensuring reliability.

1. Recordings of body position during sleep.

2. Recordings of snoring.

3. Recordings of ECG or cardiac rhythm.

4. Recordings of airflow with nasal manometry and/or thermistors.

5. Recordings of thoracic and abdominal movements.

6. Recording of SpO_2 with pulse oximetry and maximum duration of moderate signal ≤ 3 seconds at a cardiac rhythm of ≥ 80 beats/minute.

7. Time recording.

8. Indirect recording of wakefulness/sleep.

3. Attended studies

There is attendance throughout the procedure by specialized personnel (technician or nurse). Attended full or

limited polysomnography is recommended as the study of choice for the diagnosis of OSAS as well as other sleep-related breathing disorders.

4. Unattended studies

These studies are usually performed with portable equipment, record limited number of data and they are not attended by specialized personnel. Therefore, the credibility of the method is uncertain. Unattended studies are currently not recommended for diagnostic or therapeutic purposes in sleep-related breathing disorders.

5. Nocturnal continuous polysomnographic study is a recording of nocturnal sleep with duration of at least 6 hours, which is performed for diagnostic or treatment purposes.

6. Split night polysomnography. This type of study is preserved for patients who are at moderate or severe risk of OSAS. It is time-saving and cost-effective since the diagnostic study is followed by application of CPAP during the same night. The specifications of split night study and the terms of acceptance of its results are discussed in a different section.

7. Limited daytime studies: These are studies with duration less than 6 hours, usually performed at noon. Current evidence does not fully support the generalized use of this kind of sleep study. It can be used under certain conditions for example in shift-workers or in patients who have serious reasons that do not allow night recordings.

E. Indications of polysomnography^{3,4}

1. Diagnostic studies

They are performed in order to confirm a diagnosis or determine a disorder when there is:

1.1. Clinical suspicion of OSAS

a) Patients with history of loud snoring and severe daytime sleepiness or reported apneas are at high risk of diagnosing OSAS. In the presence of occupational hazards or cardiovascular disease, a polysomnography is indicated as the first priority test. Under certain conditions, these patients can be subjected to limited polysomnography.

b) Snorers with mild daytime sleepiness and without occupational hazards or cardiovascular disease are suggested to take a sleep study as a regular medical visit (second priority).

1.2. Muscular and neuromuscular disorders, chest wall or pulmonary disorders (myopathies, kyphoscoliosis, COPD).

Patients with neuromuscular disorders or chest wall abnormalities are at risk of developing severe alveolar hypoventilation during sleep, before the development of daytime hypoventilation or right heart failure. Therefore, these patients are suggested to undertake a sleep study, especially if they report daytime symptoms attributed to sleep disturbances or hypercapnia, pulmonary hypertension or some other dysfunction develops.

Patients, who suffer from pulmonary disease (e.g. COPD) and develop complications such as right heart failure, polycythemia or hypercapnic respiratory failure disproportionately severe for the stage of the underlying disease, are very likely to have OSAS or alveolar hypoventilation syndrome. A sleep study is recommended, especially if obesity or snoring is reported.

1.3. Clinical suspicion of sleep related breathing disorder on the grounds of a well-known predisposing condition unrelated to respiratory system, such as congestive heart failure, morbid obesity, acromegaly, and neurologic disorders. These patients are advised to undertake a sleep study, especially if they report severe daytime sleepiness or cardio-respiratory deterioration that cannot be attributed to other causes.

2. Application and pressure titration sleep studies

They are used for the application and determination of functional parameters of a therapeutic appliance or in order to establish the efficacy of a new treatment method. They are extensively discussed in the respective chapter.

3. Follow-up studies

They are mentioned in the respective section.

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