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GUIDELINE

Obstructive sleep apnea and primary snoring: diagnosis☆

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Description of the evidence collection method

An active search was conducted in the PubMed/MEDLINE, EMBASE, SciELO/LILACS, and Cochrane Library databases using the following key words (MeSH terms): Epworth, Berlin questionnaire, physical examination, body mass index, circumference, Mallampati, noise, pharynx, airway, Jaw, Diagnosis, Mass Screening, Diagnostic Techniques and Procedures, Diagnostic Tests, Laboratory Techniques and Procedures, Routine; Diagnostic Equipment/standards*; Comparative Effectiveness Research, Laryngoscopy, Cephalometry, Tomography, X-Ray Computed, Magnetic Resonance Imaging, Endoscopy, Pulmonary Ventilation, Polysomnography, Actigraphy, Sleep; Monitoring, Physiologic; Monitoring Sleep Apnea Syndromes, Sleep Disorders, Sleep Apnea, Obstructive; Sleep Initiation and Maintenance Disorders, Circadian Rhythm, Sleep, REM/physiology*, Snoring, Disorders of Excessive Somnolence, Restless legs Syndrome, signs and symptoms, Fatigue, Headache, Delirium, Dementia, Amnestic, Cognitive Disorders, Mood Disorders, Fatigue Syndrome, Chronic; Questionnaires, survey Ambulatory, home care services, laboratory techniques and procedures, complications, adverse effects, Obesity, Overweight, Cardiovascular Diseases, Diabetes Mellitus, Stroke, Ischemic Attack, Transient; Gastroesophageal Reflux, Pulmonary Disease, Chronic Obstructive, Pre-Eclampsia, Pregnancy, Premature Birth, Post-menopause, Memory Disorders, Mental Disorders, Cognition Disorders, Neuropsychological Tests, Severity of Illness Index, Accidents, Traffic; Mortality.

Degree of recommendation and strength of evidence

A: Experimental or observational trials of higher consistency.
B: Experimental or observational trials of lesser consistency.
C: Case reports (non-controlled trials).
D: Opinions without critical evaluation, based on consensuses, physiological studies, or animal models.

Objective

To evaluate the diagnoses of obstructive sleep apnea and primary snoring in adults and children, focusing on data from medical history, questionnaires, physical examination, and laboratory tests, as well as stimulating their investigation by general practitioners and several specialists.

Introduction

Obstructive sleep apnea (OSA) is characterized by recurrent collapse of the pharynx during sleep, resulting in a substantial decrease in airflow (apnea or hypopnea). Respiratory events trigger intermittent disorders of blood gases (hypoxemia and hypercapnia) and can lead to sympathetic system activation.

Obstructive sleep apnea syndrome (OSAS) is associated with many symptoms and comorbidities, which include excessive daytime sleepiness, cognitive problems, obesity, type 2 diabetes mellitus, hypertension, exacerbation of chronic obstructive pulmonary disease (COPD), reduced quality of life, and significant increase in risk of industrial and traffic accidents. It is also considered an independent risk factor for cardiovascular disease and ischemic stroke.

Upper airway collapse during sleep is the result of an imbalance between the activity of pharyngeal dilator muscles and negative intraluminal pressure during inspiration. Factors that tend to narrow the pharynx lumen include mucosal adhesive forces, vasomotor tone, neck flexion, jaw opening and lower dislocation, force of gravity, increased nasal resistance, Bernoulli effect (the physics principle that explains the tendency of pharyngeal collapse), and increased

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dynamic compliance. Forces that dilate the pharynx include the thoracic caudal traction by increased pulmonary volume and neck extension.

Despite showing considerable variation between individuals, there are components of the disease physiopathology that have been already demonstrated, which include changes in the upper airway anatomy, variations in the capacity of the upper airway dilator muscles to respond to respiratory adversities during sleep, changes in cortical arousal threshold during an increase in inspiratory negative pressure, variations in the ventilatory control system stability, and changes in pulmonary volume.

OSAS is thought to be a progressive disease, and it is hypothesized that primary snoring and severe OSAS are opposite stages of the same disease. This pathological evolution would occur in the following chronological order: primary snoring, upper airway resistance syndrome, OSA, mild OSAS, moderate OSAS, and severe OSAS. Prompt diagnosis and appropriate treatment are important at any of these stages.

1. What is the clinical history of the patient with OSA? How important are questionnaires?

The most frequent complaints of adult patients with OSA, when compared to non-apneic patients, are the presence of snoring, nocturnal choking, excessive daytime sleepiness (EDS), impotence, and nocturnal apneas reported by companions ($p < 0.05$)[1] (B). Other common symptoms include morning headaches, unrefreshing sleep, fatigue, and cognitive alterations.

Snoring and nocturia are common complaints in OSA[2] (B). Other clinical parameters such as body mass index (BMI), age, and gender are evaluated in Table 1. Men and women aged > 50 years diagnosed with OSA did not differ regarding the nature or severity of symptoms, as assessed by polysomnography (PSG) or the complaints of snoring, EDS, and perception of impaired diurnal function[3] (A).

Associating the subjective impression, which includes the clinical history, with physical examination and the PSG result of the apnea-hypopnea index (AHI) > 10 h allows for increased diagnostic certainty of OSA[1] (B).

To differentiate patients with and without apnea among snorers, the presence of OSAS (witnessed apnea, nocturnal choking, morning headache, or EDS) and alterations in the Epworth sleepiness scale (ESS), which must be ≥ 15 and BMI ≥ 28 kg/m^2, are assessed. The sensitivity to identify non-apneic individuals was 93.4% and the specificity was 60% ($p < 0.001$)[4] (B). This association of criteria is the best way to attain the clinical diagnosis of OSAS. When considering the disease prevalence of 15%, the presence of this association of criteria increases disease probability from 15% to 29% of cases, requiring complementary diagnostic confirmation by PSG.

Developed as a screening method for the detection of patients at high risk of OSA in primary care centers, the Berlin Questionnaire (BQ) (Box 1) has a sensitivity of 69% to 86% and specificity of 56% to 95% (positive predictive value of

Table 1 Signs and symptoms suggestive of obstructive sleep apnea (OSA) and their respective likelihood ratios that contribute to the OSA diagnosis.

	S	SP	PPV	LR+
Snoring in adult[2] (B)	82.6%	43%	59%	1.45 (95% CI: 1.20-1.76)
Nocturia[2] (B)	84.8%	22.4%	52%	1.09 (95% CI: 0.96-1.25)
Snoring and nocturia[2] (B)	97.4%	12.4%	53%	1.11 (95% CI: 1.03-1.21)
BMI > 30[2] (B)	48.1%	68.6%	61%	1.53 (95% CI: 1.07-2.19)
Age ≥ 50 years[2] (B)	52.1%	67.6%	62%	1.61(95% CI: 1.14-2.26)
Male[2] (B)	58.6%	69.5%	65%	1.89 (95% CI: 1.35-2.64)
Female[2] (B)	41.4%	30.5%	37%	0.59 (95% CI: 0.45-0.78)
Subjective impression (HC and EF)[a] (B)	60%	63%	62%	1.62 (95% CI: 1.20-2.19)
OSAS symptomsa + ESS ≥ 10 + BMI (B)	93.4%	60%	70%	2.35[a] (95% CI: 1.84-3.00)
Snoring in children[21] (B)	64%	57%	60%	1.49 (95% CI: 1.14-1.95)
Subjective impression in children[20] (B)	68.4%	59.5%	63%	1.70 (95% CI: 1.29-2.24)
SDB +EDS symptoms + learning disorders[20] (B)	8.7%	98.9%	90%	9.0[a] (95% CI: 1.16-69.73)

S, sensitivity; SP, specificity; PPV, positive predictive value; LR+, positive likelihood ratio; BMI, body mass index; SDB, sleep-disordered breathing.
[a] Obstructive sleep apnea syndrome (OSAS) symptoms: snoring, nocturnal choking, EDS, apneas witnessed by others, morning headache, fatigue, and cognitive alterations.

77% to 96%)[5-9] (B). However, for the assessment of patients in sleep centers, it did not indicate favorable results due to high rates of false-positive and false-negative results, with a sensitivity of 61.5% to 62% and specificity of 22.6% to 43%, not allowing for an increase in diagnostic certainty10,11 (B). The validation of the Brazilian Portuguese version of the BQ in sleep centers identified 68.4% of the studied population as high-risk for OSA and 31.6% as low-risk. The sensitivity and specificity values of the BQ change in relation to AHI, but even in patients at high-risk for OSA, the altered BQ has a positive likelihood ratio (LR +) of 1.44 to 1.49[12] (A).

There is an association between alterations at the BQ in the population at high risk for OSA and patients with systemic arterial hypertension (SAH) resistant to clinical treatment[13] (B). Having SAH resistant to clinical treatment is a risk factor for OSA in the Brazilian population, with a sensitivity of 44% (31% to 58%), specificity of 91% (77% to 97%), increasing the diagnostic certainty of OSA from 15% to 46% (LR+ = 4.89; 95% CI: 2.52-9.47)[14] (A)[15] (B).

The ESS validated for Brazilian Portuguese16 (B) (Box 2), is very important in the identification of EDS (ESS > 10), assisting in the screening of patients with OSAS, mainly when associated with other clinical parameters[4,10,17,18] (B). Patients with ESS scores > 10 have a 2.5-fold higher risk of having OSA when compared with a normal test[17] (B). The prevalence of sleepiness (ESS > 10) increased with OSA severity, ranging from 21.4% (AHI < 5/h) to 40.2% (AHI > 30/h) ($p < 0.001$). However, less than half of patients with moderate to severe OSA reported somnolence (45.7%)19 (B). The scale has a sensitivity of 48% and specificity of 67%, providing a LR+ = 1.45 (1.03-2.06)[9] (B).

In children with sleep-disordered breathing (SDB), most associated symptoms are snoring, EDS, learning disorders, as well as somnambulism and somniloquy. Children with report of loud and frequent snoring have a 3.5-fold higher chance of having SDB, and children with EDS have a higher chance of presenting learning disorders and of male gender. The combination of the symptoms snoring or EDS with learning disorders has high specificity (97% and 98.9%, respectively), but low sensitivity (8.7% and 4.4%, respectively)[20] (B).

In preschoolers, the presence of snoring often or almost always has sensitivity of 64% and specificity of 57%[21] (B). Clinical evaluation has sensitivity of 68.4% and specificity of 59.5% for the diagnosis of OSA in children[22] (B).

Box 1 Berlin Questionnaire; LR+ 1.44 – 1.49[20] (B).

Category 1

1. Do you snore?
( ) Yes
( ) No
( ) Don't know

2. Your snoring is:
Slightly louder than breathing?
As loud as talking
Louder than talking?
Very loud - can be heard in adjacent rooms?

3. How often do you snore?
Nearly every day
3-4 times a week
1-2 times a week
Never or nearly never

4. Has your snoring ever bothered other people?
( ) Yes
( ) No

5. Has anyone noticed that you quit breathing during your sleep?
Nearly every day
3-4 times a week
1-2 times a week
Never or nearly never

Category 2

6. How often do you feel tired or fatigued after your sleep?
Nearly every day
3-4 times a week
1-2 times a week
Never or nearly never

7. During your waking time, do you feel tired, fatigued or not up to par?
Nearly every day
3-4 times a week
1-2 times a week
Never or nearly never

8. Have you ever nodded off or fallen asleep while driving a vehicle?
( ) Yes
( ) No

Category 3

9. Do you have high blood pressure?
( ) Yes
( ) No
( ) I don't know
BMI =

Scoring of questions: Any assigned response is considered positive.
Score categories: Category 1 is positive with two or more positive responses to questions 1-5; Category 2 is positive with two or more positive responses to questions 6-8; Category 3 is positive if the answer to question 9 is positive or BMI > 30. Final result: two or more positive categories indicate high risk for OSA.

Box 2 Epworth Sleepiness Scale – Brazilian Portuguese validation. LR±1.45[9] (B).

Name: _____

Date: _____ Age (years): _____

Gender: _____

How likely are you to doze off or fall asleep in the situations described below, in contrast to feeling just tired? This refers to your usual way of life in recent times. Even if you haven't done some of these things recently try to work out how they would have affected you. Use the following scale to choose the most appropriate number for each situation:

0 = would never doze;
1 = slight chance of dozing;
2 = moderate chance of dozing;
3 = high chance of dozing

Situation	**Probability of dozing**			
Sitting and reading	0	1	2	3
Watching TV	0	1	2	3
Sitting, inactive in a public place (e.g. a theater, lecture or a meeting)	0	1	2	3
As a passenger in a car for an hour without a break	0	1	2	3
Lying down to rest in the afternoon when circumstances permit	0	1	2	3
Sitting and talking to someone	0	1	2	3
Sitting quietly after a lunch without alcohol	0	1	2	3
In a car, while stopped for a few minutes in traffic	0	1	2	3

Thank you for your cooperation

Children with symptoms of SDB may have more EDS (OR = 2.2; 95% CI: 1.7-2.8) and behavioral problems, including hyperactivity (OR = 2.5; 95% CI: 2.0-3.0), attention deficit disorder (OR = 2.1; 95% CI: 1.7- 2.6), and aggression (OR = 2.1; 95% CI: 1.6 -2.6)[23] (B). They may also have alterations in growth, central auditory processing, and nocturnal enuresis[24,25] (C).

Table 1 compares the diagnostic values of different signs and symptoms suggestive of OSAS. The higher the positive likelihood ratio (LR+), the better. For example: a LR+ = 9 signifies that children with symptoms of SDB, EDS, and learning disorder have a nine-fold higher chance of having a confirmed diagnosis of OSA.

Recommendation

There is an increased likelihood of OSA diagnostic certainty in adults when the presence of symptoms is associated with alterations in ESS and increase in BM[I4] (B), whereas in young children the clinical diagnosis of OSA is associated with the presence of SDB symptoms, EDS, and learning disorders[20] (B), as highlighted by the a in Table 1, indicating a 2.3-fold and a nine-fold higher chance of OSA diagnosis, respectively.

The main symptoms of adult patients with OSA are snoring, nocturnal choking, EDS, impotence, and reporting of apneas by companions[1] (B). The combination of snoring with nocturia can be used in OSA screening[2] (B). There are differences between men and women older than 50 years regarding the nature and severity of symptoms[3] (A). Patients with SAH resistant to clinical treatment are more likely to have OSA; thus, they should always be assessed to rule out the disease[14] (A) [15] (B).

Children with SDB are more likely to have behavioral problems, including hyperactivity, attention deficit, aggression[23] (B), and enuresis[24,25] (C), as well as alterations in growth and central auditory processing[24,25] (C).

The Berlin Questionnaire (BQ) helps in the screening of patients at high risk of OSA in primary care centers[5-8] (B), but it does not allow for a definite diagnosis of OSA by itself[12] (A).

The ESS, along with other clinical parameters, helps to identify patients with OSA[4,10,17,18] (B). Although the prevalence of ESS > 10 increases with OSA severity, less than 50% of patients with moderate to severe OSA have ESS > 10[19] (B). The diagnostic contribution of the questionnaires is similar for both ESS and the BQ, with 1.45- [9] (B) and 1.44-1.49-fold[12] (A) higher chances of disease when the questionnaire results are altered, respectively.

2. What are the most important findings during physical examination of patients with OSA and primary snoring?

The most relevant findings of the physical examination in adult patients with snoring/OSAS are obesity and alterations in the craniofacial skeleton and upper airways (UAs).

In addition to older age (> 50 years11)[26] (B) and male gender[26-28] (B), obesity markers, particularly increased BMI and neck circumference, are the main predictors of OSA presence[1,26-30] (B); however, the association between the degree of obesity and OSAS severity is still controversial[31,32] (B).

Using the AHI > 10/h, the prevalence of OSA in white men is 3.9%, while in women is 1.2%, maintaining statistically significant male:female ratio of 3.3:1 ($p < 0.0006$). This prevalence is modified when studying premenopausal women (0.6%) or postmenopausal women using hormone replacement therapy (0.5%); postmenopausal women with-

out hormone replacement present values that are similar to those in men (2.7%)[33] (A). In an epidemiological study conducted in the city of São Paulo, using clinical and polysomnographic criteria, the prevalence of OSA was 32.9% (95% CI: 29.6-36.3%), while maintaining independent associations in men (OR = 4.1; 95% CI 2.9-5.8), obese individuals (OR = 10.5; 95% CI: 7.1-15.7), and postmenopausal women (OR = 21; 95% CI: 1.4-3.9). There is an increase in OSA with increasing age, reaching an OR = 34.5 (95% CI: 18.5-64.2%) when compared with Brazilian groups aged 60-80 years to groups aged 20-29 years[30] (B).

BMI < 32.3 kg/m^2 was associated with OSAS of 0.4% (95% CI: 0.1-1.2), and BMI ≥ 32.3 kg/m^2 was associated with OSAS of 4.8% (95% CI: 2.5-9.0)[33] (A). When using BMI ≥ 32.3 kg/m^2 in the assessment of the physical examination of patients with snoring/OSA, a sensitivity of 92.5% (95% CI: 89.3%-95.8%) and specificity of 73.9% (95% CI: 61.2%-86.6%) were observed, increasing the LR+ from 1.5[32] (B) to 3.54[28] (B).

The neck circumference alone has a sensitivity of 60.6% (95% CI: 54.6 to 66.6%) and specificity of 93.4% (95% CI: 86.3%-100%), providing LR+ of 10.00 (95% CI: 4.53-22.07), increasing diagnostic probability from 15% to 64%[28] (B). The association of age > 50 years, neck circumference > 40 cm, and ESS > 10 increases the diagnostic certainty of OSA from 15% to 80% of cases. When applying the Kushida morphometric model to the Brazilian population, it was observed that the mean value of 36.7 cm (31 to 43 cm) can distinguish apneic from non-apneic individuals; in the sample studied, apneic individuals had a mean neck circumference of 40.4 cm (with a standard deviation of 4.1 cm), ranging from 31 to 54 cm[34] (B).

Through a morphometric model that associates BMI, neck circumference, and evaluation of craniofacial skeleton, considering a result found > 70, a sensitivity of 97.6% (95% CI: 95%-98.9%) and specificity of 100% (95% CI: 92%-100%) were observed. The morphometric model provides a LR+ = 97 (95% CI: 13.79-682). The use of this morphometric model should be encouraged, as it increases the likelihood of disease from 15% to 95% of cases[28] (B). In the Brazilian population, the morphometric model maintained the score > 70[34] (B).

Craniofacial alterations more often related to OSAS are those caused by maxillary and/or mandibular hypoplasia (Fig. 1), which can be identified by physical examination and confirmed by cephalometry[28,35,36] (B). In the Brazilian population, class II dental occlusion (retropositioned lower dental arch) was observed in 26.3% of cases, alterations in the hard palate (narrow or ogival) in 25.1% of cases, and mandibular hypoplasia in 19.7% of cases[36] (B) (Fig. 2).

Several anatomical alterations in the upper airways are described in patients with OSA. The most common findings are: nasal alterations; hyperplastic tonsils (Fig. 3); modified Mallampati index classes III and IV (Fig. 4) (inadequate association between the base the tongue and the oropharynx); and alterations in the soft palate, uvula, and tonsillar pillars[1,32,36,37] (B). In a Brazilian study, the most frequent findings in patients with OSA were the alterations in the soft palate (43.0%), modified Mallampati index classes III and IV (78.8%), abnormal tonsillar pillars (30.9%), uvular alterations (34.5%), septal deviations grade III (5.8%), and turbinate hypertrophy (49.8%)36 (B). The combination of BMI, modified Mallampati index, and presence of abnormal

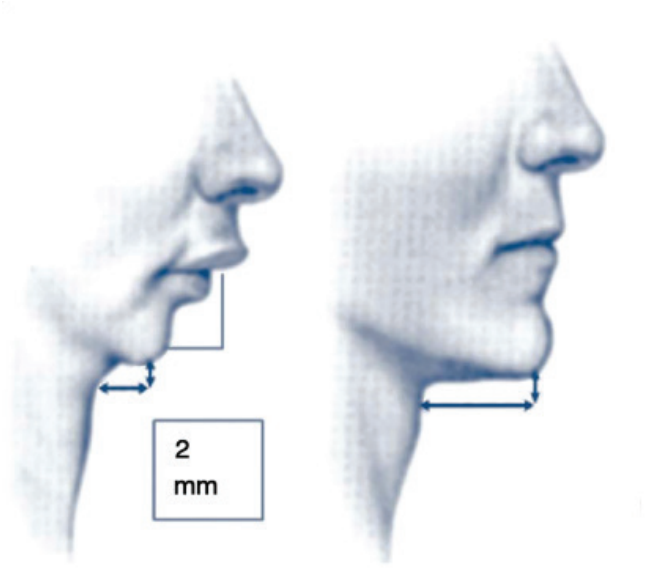

Figure 1 Retrognathia.

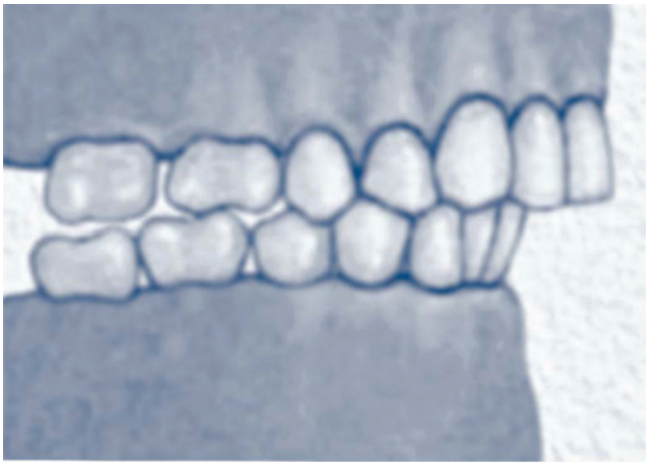

Figure 2 Class II dental occlusion (Angle).

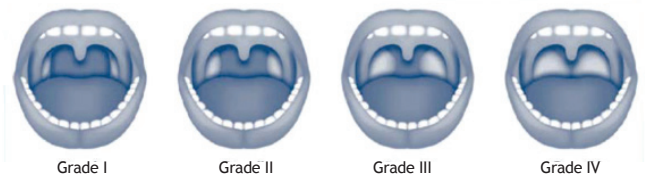

Figure 3 Grading system for palatine tonsils.

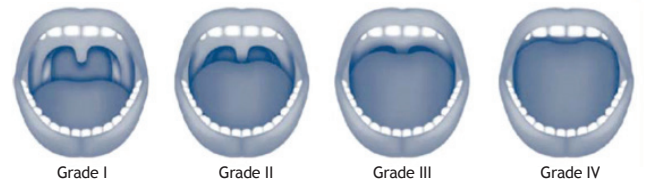

Figure 4 Modified Mallampati index.

pharynx anatomy are related to OSA presence and severity in Brazilians[38] (B).

Thus, it can be stated that patients with OSA are more obese and have higher values of neck circumference than control patients; however, the more obese patients do not always manifest more severe disease[31,32] (B). The prevalence of OSA in patients with class III obesity was shown to be greater than in the general population[32] (B). In a study in the Brazilian population, significant predictive factors for OSA in class III obese individuals were: mean age 44.6 ± 10.6 years and increased neck circumference, with a mean of 44.6 ± 5.2 cm[32] (B).

Recommendation

On physical examination of patients with snoring/OSA, the following factors must be taken into consideration: neck circumference measurements[28] (B), male gender[26-28] (B), (as there is a 3.3:1 ratio of men: pre-menopausal woman)[33] (A), older age (> 50 ± 11 years)[26] (B), and BMI values[28] (B). The most significant individual finding at the physical examination in patients with snoring/OSA is the neck circumference measure. The most relevant association in the physical examination includes BMI, neck circumference, and craniofacial skeleton assessment, called the morphometric model[2,28,34] (B). At the evaluation of the craniofacial skeleton, the anatomical alterations in the upper airways (UAs)[1,32,36,37] (B) and craniofacial abnormalities[28,35,36] (B) must be investigated. It is important to recall that patients with OSA are more obese, but the association between the degree of obesity and OSA severity is still controversial[31,32] (B).

3. When should PSG evaluation be indicated?

PSG is a complementary test considered to be the gold standard, supporting the diagnosis and follow-up of OSAS[39] (B). Depending on the parameter alteration found during the examination, there will be different diagnostic probabilities, as described in Table 2. Overall, PSG provides a diagnostic certainty of 20% in a population with low prevalence of the disease (primary care with an estimated prevalence of 4%), while in the tertiary care population, with an estimated prevalence of 15%, the diagnostic certainty reaches 54% if AHI > 10[39,40] (B). The variability between nights of sleep can show conflicting results when the same patient is being monitored, which does not rule out the need for a new examination[41,42] (B). The AHI correlation between two PSG assessments in the same patient at 30-day intervals is poor (r = 0.44)[41] (B), and this variability of single-night PSG has an impact on diagnosis; in practice, approximately 13% of patients benefit from undergoing a second PSG assessment[42] (B). Since the PSG cannot confirm the diagnosis of OSA alone with AHI ranging from 5 to 15, it is necessary to associate the PSG results with the medical history and physical examination findings. Associating the subjective impression, which includes the medical history with physical examination and the PSG result of AHI > 10 h allows for an increase in the diagnostic certainty of AOS[1] (B). Considering the population with a low prevalence of the disease, this increases the likelihood from 4% to 28%, and when the population has a pretest prevalence of 15%, there is a 63% disease probability. In primary care, patients with neck circumference > 40 cm and PSG alterations will have an increase in the probability of disease from 20% to 71%. In tertiary care, patients with the same alteration in neck circumference and PSG alterations will demonstrate an increase in the probability of disease from 54% to 91%.

PSG can confirm the diagnosis of OSA alone when the AHI ≥ 15; however, this AHI value seldom appears alone, as it is often associated with BMI and neck circumference alterations[29] (B).

Epidemiological data including age range and gender show a higher prevalence of OSA in men with AHI > 15/h with OR = 2.7 (95% CI: 2.34-3.12)[29] (B) and age ≥ 50[26] (B).

Predictive factors obtained from the history and physical examination are suggestive of the presence of OSA, but the disease diagnosis with data concerning their intensity will only be attained by monitoring the patient's sleep, even in snoring patients[43] (B).

The presence of EDS investigated by ESS correlates with an increase in apneic episodes at the PSG (AHI < 5 in 21%, AHI > 5 in 28%, and AHI ≥ 30 in 35% of cases)[23] (B). A study that evaluated the ESS in 6,440 patients reported EDS (ESS > 10) in 1,149 patients (46%) with an AHI ≥ 15[19] (B).

The presence of snoring has been associated to the OSA diagnosis, presenting a sensitivity of 97.4%, specificity of 40%, positive predictive value of 82.3%, and negative predictive value of 84.2% for moderate to severe OSAS in a group with BMI > 25[44] (B). There is an association of EDS (ESS > 10) and frequent snoring (more than six nights a week) in patients with AHI > 15[45] (B).

In the presence of arterial hypertension, the correlation with severe OSA (AHI > 30) increased to 67% and, compared with patients with AHI < 15, an OR = 2.27 (95% CI: 1.76-2.92) was observed[46] (B). Another study demonstrated a correlation between severe OSAS in patients with BMI > 30[47] (B).

Table 2 Diagnostic probability by PSG during part of the night[39] (B).

	S/SP	LR+	Diagnostic certainty (First consultation)	Diagnostic certainty (Third consultation)
GLOBAL PSG (AHI+ oximetry)	66.5%-88.7%	6.06 (95% CI: 3.41-10.77)	20%-19%	52%
Only AHI > 5	69.7%- 87.4%	5.77 (95% CI: 3.35-9.97)	21%	50%
Only AHI >10	79.5%-86.7%	6.08 (95% CI: 3.63-10.18)	9%	54%
Only OXIMETRY	87.4%-64.9%	2.51 (95% CI: 1.90-3.31)		31%

Obesity measured by BMI has been frequently associated with OSAS. Studies indicate that AHI worsens with increasing BMI[26,44] (B) and demonstrates an association of OSAS in patients with BMI > 35[48] (B).

Recommendation

PSG should be indicated in patients with clinical suspicion of OSA and the presence of snoring[44,45] (B) associated or unassociated with EDS assessed by ESS[19,23] (B), neck circumference > 40 cm, obesity[26,44,48] (B), and arterial hypertension[46] (B), especially in the context of difficult-to-control hypertension[14] (A)[15] (B). The variability between nights of sleep sometimes requires the performance of a second PSG[41,42] (B).

The differential diagnosis between primary snoring and OSA can only be established after sleep monitoring[39,43] (B).

4. What are the sleep monitoring modalities and when should they be requested?

There are four modalities of sleep monitoring:

- Type I
  Performed in a sleep laboratory with > seven channels for monitoring
- Type II
  Non-assisted with > seven channels for monitoring
- Type III
  Monitoring with four to seven channels
- Type IV
  Monitoring with one or two channels, of which one is oximetry

The gold standard type-I PSG examination consists of the evaluation through at least seven channels to capture the physiological variables including electroencephalogram, electromyogram (chin and tibial), electrooculogram, airflow, respiratory effort, oxygen saturation, electrocardiogram, body position, and snoring. It is performed in a sleep laboratory, assisted by a PSG technician, with a minimum of six hours of monitoring; the data are interpreted by a physician qualified to interpret a report[39,49,51] (B) [52,53] (D).

Monitoring with portable equipment is classified by the number of capture channels available in each device. These tests may be assisted by a PSG technician, allowing for the examination to be performed in the patient's home[54,56] (D). A major limitation is the loss of monitoring channels due to failure, or loosening or disconnection of sensors, which has been estimated at between 4% and 33%, and the variability of equipment and technologies involved in the test[57] (D).

Portable sleep monitoring type II (PSM II) (comprehensive) comprises at least seven channels, including electroencephalogram, chin electromyogram, electrooculogram, airflow, respiratory effort, heart rate, and oxygen saturation. It allows for the identification of the different sleep stages with demonstration of statistics and calculations of AHI/h. Its limitation is the fact that it requires the technician to go to the patient's residence to set up the equipment and remove it on the following day, but if a channel is disconnected during the examination, there is no replacement[54-56] (D) [57] (D). PSM type II has shown similar results for AHI during at-home monitoring when compared to laboratory assessment[58] (B). It is estimated to have 70% of sensitivity and 91% of specificity[59] (B).

Portable monitoring type III (cardiopulmonary) uses between four and seven channels, including oxygen saturation, airflow, respiratory effort, and heart rate. It does not assess sleep stages and does not differentiate whether the events occur during the periods of wakefulness or sleep. It demonstrates and differentiates only respiratory events, not allowing for the diagnosis of other events, such as lower-limb movements. Some devices can be set up by the patient at home, without the need for a technician[55-57] (D)[58] (B). In a study of Brazilian patients, when indices were compared to type I monitoring, they showed results with strong correlation, with r = 0.876 (95% CI: 0.81-0.91; p < 0.0001) for any value of AHI (> 5, > 15, and > 30)[60] (A). Another equipment model presented similar results[61] (B).

Type IV monitoring uses one to two channels, and one of them must be oximetry. It does not assess sleep stages and does not differentiate between apnea types, but demonstrates desaturation. It does not allow for the evaluation of any data related to sleep[55-57] (D)[58] (B). In a study with Brazilian patients, similar results were observed when comparing the Type IV portable monitoring performed either in the sleep laboratory or at home[62] (A). Considering the high prevalence of OSA (33% in the population of São Paulo, SP, Brazil)[30] (B), type IV portable monitoring increases the disease likelihood to 57%[62] (A). Using the same type of equipment, studies have compared the rates of AHI with type 1 PSG and observed significant correlations, with r = 0.9563 (B) and r = 0.895[64] (B). Due to the fact that it is easy to repeat, three assessments were performed with a portable monitor on three consecutive nights, with no significant differences found between the values in these three examinations[63] (B).

The indication for type III and IV monitoring are still restricted to patients with high probability of OSA, whose assessment is based on anamnesis, physical examination, and questionnaires. If these types of monitoring do not diagnose OSA, type I or II monitoring is indicated to rule out a false negative result[56,57] (D).

PSG for titration of positive airway pressure (PAP) implies that the patient will return for a new sleep monitoring, assisted by technician in a sleep laboratory. The choice of treatment with PAP requires the identification of values at which the pressure produced by the machine can eliminate respiratory events. There is a protocol for the gradual increase in positive pressure associated with the placement of appropriate interfaces (mask). The correct PAP equipment to be used by the patient, with pressure identified by titration and the type of mask to be used, is indicated only after the titration[65,66] (D).

The choice of treatment with PAP means the indication of a long-term treatment. Measures of adherence to long-term treatment also depend on the type of titration to which the patient was submitted. The comparison of manual titration with automatic titration (both in the laboratory) has been discussed, but the results are still of short-term and without significant differences[67] (B). When comparing the two methods, it can be observed that both allow for improvements in AHI and sleepiness (ESS), with no differences in sleep architecture and treatment concordance, but with differences in treatment adherence[68] (B).

Split-night PSG in the first half of the night for the diagnosis and second half for PAP titulation. This modality does not allow for an accurate patient diagnosis, as it interrupts the evaluation halfway through the night and attempts to find the adequate pressure for the treatment in only half of the night. It should not be an elective procedure[53,65,66] (D).

The initial adherence to PAP comparing the titration of the whole night with the split-night shows similar results when comparing the number of days (78.7 *vs.* 77.5%), night hours of use (3.9 *vs.* 3.9 hrs), percentage of nights with use > four hours (52.9% *vs.* 51.8%)[69] (B).

When performing a diagnostic investigation of OSA, the intention is to attain 75% or more of diagnostic certainty[70] (D). Considering that the association of clinical and supplementary examination still estimates the probability of disease between 25% and 75%, the investigation should be continued, adding other diagnostic methods.

The disease prevalence before the examination interferes with the diagnostic certainty in the presence of any altered results; Table 3 compares the diagnostic possibility among the four modalities of sleep monitoring, differentiating pre-testing low prevalence from high prevalence. There is a likelihood of OSA diagnostic certainty ≥ 75% when using only PSG I and PSG II in adult populations with high disease prevalence estimated at 32.9%[30] (B). Table 4 associates several diagnostic methods, such as signs and symptoms, physical examination, and two types of PSG (I and IV) in a population with low disease prevalence estimated at 4%[33] (A) in order to achieve diagnostic confirmation (diagnostic certainty > 75%*). A male individual who snores does not demonstrate diagnostic certainty of OSA, even after PSG I is performed; similarly, a male obese individual does not demonstrate diagnostic certainty OSA, even after PSG I, as described in Table 4. In these two cases, before performing the first PSG, the neck circumference or the morphometric model should be investigated, as they both have a high positive likelihood ratio[28] (B), increasing diagnostic certainty. It may be necessary to perform the second PSG, due to AHI variability[41,42] (B). However, a thin male individual, younger than 50 years, with symptoms of OSA, neck circumference > 40 cm, and difficult-to-control hypertension is 76% certain to develop the disease, regardless of the PSG results (Table 4).

Recommendation

Monitored full-night PSG performed in a sleep laboratory is considered the gold standard for OSAS diagnosis[39,49,51] (B). The diagnostic probability is similar when performing PSG I and II, as described in Table 3. Portable sleep monitoring assessments still have the limitation of monitoring channel loss due to failure, or loosening or disconnection of sensors[57] (D), and the need to perform a new PSG I or II to rule out false negatives in cases of high disease probability and normal initial monitoring results[56,57] (D).

The choice of treatment with PAP implies a monitored full-night PAP titration performed in a sleep laboratory by a PSG technician[65,66] (D). There are no significant differences in positive pressure tolerance time during the night, daytime sleepiness improvement, overall improvement, and patient satisfaction when comparing the whole-night PAP titration assisted by a technician with automatic titration[69-71] (B), but there are controversies regarding treatment adherence[67,68] (B).

Table 3 Diagnostic probability by polysomnography (PSG).

	S/SP	LR+	Diagnostic certainty (First consultation)	Diagnostic certainty (Third consultation)
GLOBAL automated PSG[49] (B) (AHI + oximetry)	85%-93%	12.14 (95% CI: 5.92 -24.93)	34%	86%
Split-night PSG (in patients already with AHI > 20)[50] (B)	93%-95%	18.60 (95% CI: 7.90-43.78)	-	90%

Table 4 Sleep monitoring methods and diagnostic probability according to the prevalence of the population.

	S	SP	LR+	LP	HP
PSG I (part of the night and evaluation of all parameters)[39] (B)	66.5%	88.7%	6.06 (95% CI: 3.41-10.77)	20%	75%*
PSG I (full- night with automated analysis)[49] (B) PSG II[59] (B)	85%	93%	12.14 (95% CI: 5.92-24.93)	34%	86%*
PSG II[59] (B)	70%	91%	7.78 (95% CI: 4.12-14.70)	24%	79%*
PSG III (when AHI > 5)[60] (A)	93%	59%	2.27 (95% CI: 1.78-2.89)	09%	53%
PSG III (when AHI > 15)[60] (A)	85%	80%	4.25 (95% CI: 2.85-6.34)	15%	68%
PSG IV (at home)[62] (A)	96%	64%	2.7 (95% CI: 2.05-3.47)	10%	57%

Table 5 Examples of association of signs and symptoms, physical examination, and polysomnography to diagnose OSAS in a population with low prevalence of disease (estimated at 4%).

	Gender	Snoring	PSG I[49] (B)	Diagnostic certainty
Male + snoring + PSG I	1.89	1.45	12.14	60%
Female + snoring + PSG I	0.59	1.45	12.14	35%
Male + snoring + PSG IV	1.89	1.45	2.7	40%
Female + snoring + PSG IV	0.59	1.45	2.7	37%
BMI				
Male + BMI > 30 + PSG I	1.89	1.53	12.14	62%
Male + BMI > 30 + PSG IV	1.89	1.53	2.7	40%
Age > 50 years				
Male + age > 50 years + PSG I		1.89	12.14	60%
Male + age > 50 years + PSG IV	1.89	1.61	2.7	40%
Male + age > 50 years + OSAS symptoms + ESS ≥ 10 + BMI + PSG I	3.5	1.61 2.35 (OSAS+ ESS+BMI)	12.14 (PSG I)	78%[a]
Male + age > 50 years. + OSAS symptoms + CC	(male > 50 yrs.)	1.62 (OSAS)	10.00 (CC)	67%
+ OSAS symptoms + CC+ difficult SAH	3.5 (male > 50 yrs.)	1.62 (OSAS)	10.00 (CC) 4.89 (HAS)	76%[a] (diagnostic independent from PSG)
Male + age > 50 years . + OSAS symptoms + CC + BMI	3.5 (male > 50 yrs.)	1.62 (OSAS)	1.53 (IMC) 10.00 (CC)	76%[a] (diagnostic independent from PSG)
Male + age > 50 years + OSAS symptoms + CC + PSG I	3.5 (male > 50 yrs.)	1.62 (OSAS)	12.14 (PSG I) + 10.00 (CC)	96%[a]
Male + age > 50 years + OSAS symptoms + ESS ≥ 15 + BMI + CC + PSG I	3.5 (male > 50 yrs.)	2.35 (OSAS + ESS+BMI)	12.14 (PSG I) + 10.00 (CC)	97%[a]

5. When should PSG be requested in children?

OSA in children has important conceptual, etiological, and classification differences when compared to adult apnea.

Snoring is a common complaint reported by the parents; however, the differentiation between primary snoring and OSA in children cannot be made solely based on clinical history data[21,72,73] (B). When comparing primary snoring with OSA, statistically different variations can be observed, such as daytime mouth breathing (61% *vs.* 85%, p = 0.024), witnessed apnea (46% *vs.* 74%, p = 0.013), and respiratory effort (58% *vs.* 89 %, p = 0.003), but without enough strength to confirm the diagnosis of OSA[73] (B).

The presence of syndromic pictures, neuromuscular disease, and obesity are factors to be considered when requesting PSG assessment in children. Differentiation of pictures of central origin and estimation of apnea severity are important in the prevention of preoperative complications in children after tonsillectomy. Moreover, tonsillar size is not always a good indicative of the need for surgical intervention, and often, parents do not want to the child to undergo surgery and thus underestimate the child's symptoms[74] (D).

Table 6 shows the sensitivity, specificity, positive predictive value, and negative predictive values of the most common symptoms in children[75] (B).

Normal values for PSG in healthy children aged 1 to 15 years are: AI < 1.0 with maximum desaturation of 89%; expiratory PCO_2 cannot be > 45 mmHg for more than 10% of total sleep time[76] (B).

The American Academy of Sleep Medicine believes that the criteria of normality can be used up to the age of 18 years[77] (D). Studies have demonstrated that between 13 and 18 years, there is a difference when using the AHI criteria recommended for children and those recommended for adults, but this difference does not result in significant changes in the classification of OSA severity when the alternative criteria for adults are used[78] (B).

The presence of OSA has increased and is recognized as a cause of morbidity, even in young children, with an estimated prevalence of 1% to 4%. Its diagnosis is important, as lack of treatment leads to learning and memory difficulties and decreased weight and height growth rates. In the long-term, it increases the risk of hypertension and depression[79] (D).

Recommendation

PSG is recommended for all children with frequent snoring and who need to be differentiated from patients with OSA[21,72,73] (B). For the diagnosis of OSA, AI > 1, with satura-

Table 6 Sensitivity, specificity, positive predictive value, and negative predictive value of symptoms in children[75] (B).

		Sensitivity	Specificity	PPV	NPV
Symptoms	Present	%	%	%	%
Snoring	Sometimes	78	36	61	55
	Always	95	13	68	55
Difficulty breathing	Sometimes	81	30	54	57
	Always	90	33	77	57
Witnessed apnea	Sometimes	59	46	61	44
	Always	55	79	85	44

tion < 89% and/or expiratory PCO_2 > 45 mmHg for over 10% of total sleep time are considered diagnostic criteria[76] (B).

The AHI criteria established for children may be used up to the age of 18 years[77] (D). Between the ages of 13 and 18 years, the criteria recommended for children or the alternative criteria for adults may be used without change in OSAS classification[78] (B).

6. What is the importance of supplementary examinations in the investigation of OSA and snoring?

There are other relevant, currently available tests for the evaluation of OSA and snoring, in addition to the gold standard (PSG). Among them are sleep endoscopy, video-nasofibrolaryngoscopy with Muller's maneuver, magnetic resonance imaging (MRI) and computed tomography (CT) of the upper airways, and cephalometry[80-90] (B).

Much has been discussed regarding the real importance of sleep endoscopy, which is the visualization of the upper airway through a flexible nasal endoscope during pharmacologically-induced sleep, to aid in the topographic diagnosis of snoring and OSA. When comparing patients with OSA using flexible video-nasofibrolaryngoscopy in wakefulness and during sleep endoscopy, aiming at the visualization of the pharyngeal obstruction site, similar results can be observed between the two tests in only 25% of cases. There was obstruction in the hypopharynx during pharmacologically-induced sleep in 33% of cases[80] (B).

Another study, comparing sleep endoscopy and video-nasofibroscopy with Muller's maneuver, showed that the surgical indication during wakefulness was 74%, whereas it was 54% at the sleep endoscopy analysis, corroborating the lack of agreement between examinations[81] (B). Patients with OSA who were using intraoral mandibular advancement devices underwent sleep endoscopy with and without the use of these devices. It was observed that patients who used the device (only those with successful treatments were evaluated) had a significantly increased upper airway area[82] (B).

When comparing the modified Mallampati index (MMI) of patients with primary snoring and OSA through sleep endoscopy, it was observed that there was no linear association between the obstruction level at the sleep endoscopy and the MMI. Patients with larger tongues (MMI 3 or 4) did not present narrowing at the region of the base of tongue; of this group, 76% had obstruction in the retropalatal region[83] (B).

Sleep endoscopy is not significantly relevant for the topographic diagnosis of OSA, which does not indicate irrelevance when assessing the apneic and snoring patient. It is worth mentioning that the criticism of this examination includes the fact that sleep is induced by medications, which can alter the pharyngeal muscle tone, lack of information regarding the patient's stage of sleep , and speculation on the pharyngeal region with non-segmented anatomical structure[80-83] (B).

Muller's maneuver is quite prevalent among otolaryngologists in the evaluation of patients with snoring and obstructive sleep apnea, but its real importance has been increasingly questioned. Comparing patients with a history of snoring and patients with OSA demonstrated by the PSG, it became clear that there are no significant differences between the two groups when analyzing BMI and retrolingual and retropalatal narrowing analyzed by video-nasofibrolaryngoscopy with Muller's maneuver. However, a positive association between BMI, AHI, and retrolingual obstruction is observed when considering only the group of patients with apnea[84] (B). Video-nasofibrolaryngoscopy with Muller's maneuver was performed in the supine and standing positions in OSAS patients, scanning the images on specific software to minimize the subjectivity of evaluation, subsequently comparing the results with MRI of the pharyngeal region. There is an agreement between the two methods of 93.3% in the retropalatal and of 95.6% in the retrolingual region[85] (B). Thus, it can be observed that Muller's maneuvers do not have the capacity to significantly alter management in patients with OSA, especially because the patient is usually evaluated in a non-supine position and during wakefulness. Furthermore, it is noteworthy that there is subjectivity and lack of homogeneity during this assessment, as the inspiratory force which the patients present varies significantly and evaluation data are yet to be established.

Imaging tests such as MRI, CT, and cephalometry are non-invasive and can be objective in their results; however, their actual relevance continues to prompt studies in several reference centers in the world.

When evaluating patients with OSA and normal patients through MRI of the upper airway, no significant differences were observed between the two groups regarding the inter-

nal distance between the two mandibular condyles and the mandible bone thickness. However, patients in the apnea group have greater mandibular discrepancy, a smaller internal mandibular length, and a smaller area in the mandibular basal plane than the control group. There were no significant differences in the morphological parameters of the mandible between the obese and nonobese patients with apnea. The volumes of the tongue, soft palate, and lateral pharyngeal walls did not differ significantly between the groups[86] (B). Ultrafast MRI (0.8 s) was performed in patients with OSAS (AHI > 10) during wakefulness and sleep, and in non-apneic patients (through clinical history and nocturnal oximetry) during wakefulness. It was observed that, during part of the respiratory cycle, the velopharyngeal region is smaller in apneic patients, and that the variation in the velopharyngeal area during the respiratory cycle is greater in apneic patients, particularly during sleep, suggesting a greater plasticity of the upper airway in these patients. Furthermore, they verified that the area of pharyngeal narrowing was similar in both the anteroposterior and latero-lateral views, both in controls and in apneic individuals during wakefulness; however, during sleep, apneic individuals have maximal circular narrowing of the pharynx. There is also an inverse association between dimensions of the lateral pharyngeal walls and the airway area, probably indicating that the lateral walls are passively compliant as a result of changes in airway caliber. It was observed that the volume of the soft palate and adipose tissue in the parapharyngeal region is higher in apneic patients[87] (B).

Focusing on the upper airway CT in the evaluation of patients with sleep-disordered breathing, this imaging study was evaluated in patients with apnea (AHI > 5) and 24 primary snorers (AHI < 5) with oro- and hypopharynx measurements, and correlated with the obstructive apnea severity indices and cephalometric studies. Patients with severe OSA had significantly greater narrowing in the uvula region during expiration, more inferiorly positioned hyoid bone, larger volume of soft palate, and larger neck circumference when compared with primary snorers and patients with mild to moderate OSA[88] (B). When comparing the CT and PSG in patients with obstructive sleep-disordered breathing (1/6 with primary snoring and 5/6 with OSAS), a significant association between retropalatal and latero-lateral pharyngeal diameters with high rates of AHI was observed. It was also verified that retropalatal and retroglossal spaces were predictive of the apnea index severity. None of the CT parameters correlated with intensity of snoring and minimal O_2 saturation. BMI correlated positively and significantly with retropalatal distance and AHI. From the anatomical standpoint, the latero-lateral retropalatal view is significantly associated with impairment of the upper airway caliber in patients with sleep-disordered breathing[89] (B). When comparing the upper airway diameter by CT in patients with OSAS and healthy patients, no correlation existed between PSG parameters in obstructive sleep-disordered breathing (minimum O_2 saturation and AHI) and pharyngeal dimensions[90] (B). There were no significant differences between the tomographic measurements of the pharyngeal airway in vigil patients submitted to lateral pharyngoplasty compared to uvulopalatopharyngoplasty, although there were differences in clinical and polysomnographic results of this population; therefore, there was no correlation between polysomnographic and CT parameters in OSAS patients submitted to surgery[91] (B). Areas of the nasopharynx, oropharynx, and hypopharynx were evaluated during inspiration and expiration, as well as the diameters of the uvula and retropharyngeal tissue to compare the results obtained by CT in patients with apnea (AHI > 10) and without apnea (AHI < 10). It was observed that the retropharyngeal tissue in apneic patients presents more volume than in non-apneic patients, with 10.3 ± 3.6 mm *vs.* 6.4 ± 2.7 mm, $p < 0.01$. However, the nasopharynx areas during expiration (228.4 *vs.* 281.9 mm) and inspiration (195.9 *vs.* 300.4 mm) of the non-apneic patients were slightly larger, but without statistically significant differences[91] (B).

When studying patients with OSAS and controls by PSG and TC, in which OSAS patients had undergone uvulopalatopharyngoplasty, it was observed that severely apneic patients had a narrower sectional area of the oropharynx (50 mm^2 on average) when compared to the others. The control patients and patients submitted to uvulopalatopharyngoplasty without OSAS, i.e., with primary snoring, had minimal pharyngeal area of 110 mm^2, on average. Furthermore, patients with moderate OSAS submitted to surgery demonstrated values between 60 and 100 mm^2 (B).[91]

Cephalometry is a useful method in the evaluation of apneic and snoring patients[93] (C). The choice to request this examination as a routine investigation in a patient with OSA has been the subject of debate, since it has not been proved that it actually changes the therapeutic approach. However, it can be observed that cephalometry is crucial in the surgical planning of patients submitted to orthognathic surgery for the treatment of OSAS. The association between cephalometry and the degree of OSAS severity in adult patients with and without obstructive sleep apnea was analyzed. It was observed that the length of the upper airway was strongly correlated with the severity of OSA in men ($r = 0.72$, $p < 0.01$) and moderately associated in women with OSAS ($r = 0.52$, $p < 0.01$)[94] (C).

Thus, imaging tests, even during induced sleep, require further studies to assess the applicability of their results as auxiliary examinations when defining conducts. Currently, these tests are more relevant for the development of research in this area.

Recommendation

Sleep endoscopy is employed in the clinical investigation of apneic and snoring patients, but controversies still exist regarding its applicability in routine assessment[80-83] (B).

Flexible video-nasofibrolaryngoscopy does not change the conduct in patients with snoring and OSA, and there is no homogeneity of results among different observers[84,85] (B).

MRI and CT of the pharynx are noninvasive tests and demonstrate that apneic patients have a narrower sectional pharynx area than non-snorers and non-apneic patients, but the location of these strictures varies between individuals[87,88,90] (B).

Cephalometry is altered in apneic patients when compared to non-apneic patients, and it is essential for surgical planning in patients who will undergo orthognathic surgeries[92,93] (C).

7. What are the consequences of OSAS?

Moderate to severe OSAS is an independent predictor of all-cause mortality, with HR = 6.24 (95% CI: 2.01-19.39)[95] (A), and this association is not attributable to obesity, age, or other medical chronic conditions, especially in men with severe OSAS aged 40 to 70 years[95] (A). Mild OSAS is not an independent risk factor for all-cause mortality, with HR = 0.47 (95% CI: 0.17-1.29)[95] (A). An increased risk of coronary events or death from cardiovascular causes can be observed, regardless of other factors, in patients aged > 50 years[95] (A)[96,97] (B), with HR = 2.06 (95% CI: 1.10-3.86)[98] (A). A self-assessment by standardized questionnaire showed a greater association between OSAS and heart failure and stroke than with coronary heart disease[96] (B).

In healthy middle-aged adults and in the elderly, OSAS is associated with increased prevalence of systemic arterial hypertension. Correcting for the main confounding factors (age, gender, BMI, and other measures of adiposity), as well as other potentially relevant variables (tobacco and alcohol consumption), higher AHI and longer desaturation time < 90% were associated with higher risk of hypertension, with OR = 1.37 (95% CI: 1.03-1.83)[99] (B). Reduction in systolic dipping related to OSA severity was demonstrated: when AHI < 5, hypertension had OR = 3.1 (95% CI: 1.3-7.7), but when AHI > 15, hypertension had OR = 4.4 (95% CI: 1.2-16.31). This lack of systolic dipping can be one of the mechanisms by which OSA contributes to an increase in cardiovascular diseases[100] (B).

There is evidence that patients with OSA older than 40 years without underlying arterial hypertension may develop the disease perhaps partly due to the influence of obesity; however, in patients with AHI > 30, a small influence of OSA itself cannot be ruled out in the genesis of hypertension[46,47,99] (B).

OSAS is an independent risk factor for developing type II diabetes[101] (A)[102] (B)[103] (C), with HR = 1.4 (95% CI: 1.10-1.86), p = 0.008[101] (A).

Reduced time of sleep is associated with obesity in adults. Sleep lasting less than five hours per night is associated with central obesity and increased body fat percentage and body mass index, on average 2.5 kg/m^2 (95% CI: 2.0-2.9) for men and 1.8 kg/m^2 (95% CI: 1.1-2.4) for women[104] (B). Patients with OSAS and metabolic syndrome103 (C) and/or morbid obesity[105] (B) have increased sympathetic tone, with increased cardiovascular risk. Children and adolescents with OSAS and a BMI percentile > 85% assessed by questionnaires have lower quality of life[106] (B).

OSAS is an independent risk factor for ischemic stroke[95,107] (A), with a relative risk of death from stroke (RR) = 5.16 (95% CI: 3.72- 6.60)[108] (B). The risk is higher for men with mild to moderate OSAS[109] (B), with HR = 6 (95% CI: 2%-10%)110 (A). Menopausal women, aged 50-79 years, of whom 8.3% had sleep duration < five hours per night and 4.6% had nine hours of sleep per night, were followed-up on average for 7.5 years. There is an association between long sleep duration and risk of ischemic stroke, with RR = 1.70 (95% CI: 1.32-2.21) for those who slept nine hours a night, regardless of the presence of snoring or somnolence. There was no significant association between ischemic stroke and short sleep duration[111] (A). A reduction in daytime sleepiness and BMI was verified in patients after ischemic stroke; this population may be underdiagnosed for OSAS[95] (A).

Untreated OSAS is a contributing factor in motor vehicle accidents[112,113] (B). Treatment of OSAS with CPAP reduces the relative risk of collisions, with RR = 0.278 (95% CI: 0.22-0.35), p < 0.001[112] (B).

Sleep apnea is associated with a higher prevalence of psychiatric comorbidities such as depression (21.8%), anxiety disorder (16.7%), post-traumatic stress disorder (11.9%), and psychosis and bipolar disorder (3.3%)[114] (B).

Several studies have proposed an association between OSAS and neurocognitive dysfunction[115,116] (B). When assessing elderly individuals considered healthy for their age, with a mean age of 68 years, 58.5% females, the performance of the PSG showed that 53% had an AHI > 15 events/h and 37% had AHI > 30 events/h, of whom only 9.2% had EDS (ESS > 10). There was no significant association between AHI, nocturnal hypoxemia, and cognitive performance, except a tendency toward slower performance in patients with AHI > 30 events/h[115] (B). Mild to moderate OSAS has minimal impact on measures related to attention or speed of executive functions and processing speed when comparing OSAS individuals with the non-apneic[117] (B). OSAS may exacerbate cognitive impairment in dementia caused by Alzheimer's disease[118] (B).

Gastroesophageal reflux disease (GERD) is more prevalent in symptomatic patients with sleep-disordered breathing; however, the occurrence of gastroesophageal reflux or reflux symptoms was not significantly influenced by the severity of OSAS. There appears to be an increasing index of microarousal caused by reflux in patients with OSAS when compared to the simple snorer[119] (B).

Patients with chronic obstructive pulmonary disease (COPD) and OSAS ("overlap syndrome") have an increased risk of death and hospitalization for COPD exacerbation. At a mean follow-up of 9.4 years (3.3 to 12.7 years) patients with overlap syndrome not treated with CPAP had higher mortality when compared to those using CPAP, with RR = 1.79 (95% CI: 1.16-2.77) and increased tendency to COPD exacerbation requiring hospitalization, with RR = 1.70 (95% CI: 1.21-2.38)[120] (B).

In obese OSA patients without COPD, daytime hypercapnia is associated with OSAS severity, higher BMI, and higher mechanical restriction of the chest wall[121] (B).

Pregnant women with OSAS have higher risk of pre-eclampsia, premature birth, and medical complications[122] (C). For pregnant women with chronic snoring and hypertension, the use of nasal CPAP, while maintaining the usual prenatal care treatment, appears to improve blood pressure and prevent complications[123] (B).

Recommendation

Moderate to severe OSAS is a risk factor for mortality from any cause[95] (A). OSAS increases the risk of coronary artery disease[98] (A), type 2 diabetes mellitus[101] (A), ischemic stroke[110] (A), hypertension[47,99,100] (B), obesity[104] (B), hospitalization, and death from COPD exacerbation[120] (B). There is an association of OSAS with psychiatric comorbidities[114] (B), preeclampsia and premature birth[123] (B), in addition to contributing to automobile accidents[112,113] (B). Considering the severe consequences of OSAS, it should always be investigated to prevent underdiagnosis and treatment delay.

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