Romanian Journal of Rhinology, Vol. 3, No. 12, October - December 2013

LITERATURE REVIEW

The diagnosis of obstructive sleep apnea syndrome

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ABSTRACT

Clinically, obstructive sleep apnea syndrome (OSAS) is defined by daytime sleepiness and night-time snoring, accompanied by interruptions of breathing or awakenings due to feelings of choking consequent to obstructive respiratory events, such as apneas, hypopneas and respiratory-effort-related arousals (RERAs). It is clear that otolaryngologists are often the first to come across such patients. Therefore, it is a challenge to correctly diagnose these patients on the basis of clinical and instrumental investigations, in order to assess them for therapeutic, medical and surgical purposes. It is especially important to pay attention to the diagnostic procedure because of the relative novelty of sleep-related respiratory disorders as a pathology outside the traditional domain of expertise of ENT specialists.

The diagnostic procedure must be aimed to: compiling a thorough clinical history; evaluating, clinically and instrumentally, all alterations of normal anatomy and physiology of the cervical-cephalic regions and locating the obstruction site(s) of the upper airways.

According to the 2007 Italian Society of Otolaryngology guidelines, it is our view that patients suspected of OSAS should undergo a basic set of tests for the gathering of clinical data, to be followed by a more advanced clinical-instrumental investigation in case of surgical planning.

KEYWORDS: obstructive apnea, hypopnea, respiratory-effort-related arousals, sleep endoscopy

INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is a common disorder affecting at least 2-4% of the adult population. It is characterized by collapse of the upper airways, leading to repeated instances of airflow cessation, oxygen desaturation and sleep interruption[1].

According to the US National Commission on Sleep Disorders, more than 40 million people are affected by sleep disorders in the United States, while in 2000 it was estimated that 93% of female and 82% of male OSAS patients remained untreated[2].

Clinically, OSAS is defined by daytime sleepiness and night-time snoring, accompanied by interruptions of breathing or awakenings due to feelings of choking, consequent to obstructive respiratory events, such as apneas, hypopneas and respiratory-effort-related arousals (RERAs).

It is now clear that such terms as simple and chronic snoring, obstructive sleep apnea syndrome and "grand snorers' disease", once used to designate the same pathology, do actually deserve their own semantic independence to define different patterns of clinical signs and symptoms.

Furthermore, perusal of the literature makes it increasingly evident, thanks to more and more advanced diagnostic techniques, that sleep-related respiratory disorders are associated not only with cardiovascular pathology, such as arterial hypertension[3] (as already shown by Coccagna and Lugaresi in the 1970s[4]) , but also with systemic endocrine and neurological disorders[5].

It is clear from these premises that otolaryngologists are often the first to come across such patients. Therefore, it is a challenge to correctly diagnose these patients on the basis of clinical and instrumental investigations, in order to assess them for therapeutic, medical and surgical, purposes.

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Diagnostic procedure must be aimed to:
- Compiling a thorough clinical history;
- Evaluating, clinically and instrumentally, all alterations of normal anatomy and physiology of the cervical-cephalic regions;
- Locating the obstruction site(s) of the upper airways.

EVALUATION PROTOCOL

According to the 2007 Italian Society of Otolaryngology guidelines, it is our view that patients suspected of OSAS should undergo a basic set of tests for the gathering of clinical data, to be followed by a more advanced clinical-instrumental investigation in case of surgical planning.

Basic Test Set:
- anamnestic evaluation
- ENT clinical examination
- Muller's maneuver - assisted fiber laryngoscopy.

Advanced Clinical-Instrumental Investigation:
- Nose function trials
- Cephalometric analysis
- Sleep endoscopy
- Imaging

Given the large amount of information to be analyzed and integrated with the results from nocturnal cardio-respiratory monitoring, it is useful to adopt specially-dedicated medical records tabs for this disorder, as already suggested by several authors[6].

MEDICAL HISTORY

The compilation of a thorough medical history needs to be the first step for any ENT specialist and certainly provides the first diagnostic clue.

The history of apnea patients should consist in:
- Follow-up on any general clinical condition; this allows to detect systemically-aggravating disorders which may impact the OSAS clinical presentations (compare Overlap syndrome, resulting from OSAS interacting with alveolar hypoventilation from pulmonary disease).
- In-depth information on lifestyle habits (smoking, alcohol, sports, diet).
- Disclosure of any at-home therapeutic drug use.
- Assessment of day- and night-time symptoms by means of dedicated questionnaires (Epworth, Berlin, Stop bang), not only addressing daytime somnolence and sleep quality, but also fundamental risk factors for OSAS, particularly age, anthropometric features (e.g. BMI – Body Mass Index, neck and waist circumference) and the presence of hypertension or other systemic disorders.
- Evaluation of past ENT-related clinical history (ENT-related diseases or previous surgical interventions).

CLINICAL EXAMINATION

Traditionally, the ENT clinical examination focuses on the cervical-cephalic regions and the anatomy of the upper airways, exposing possible anomalies or disorders which may or may not be correlated with the respiratory dysfunction.

Therefore, the examination needs to be performed as usually done for any ENT visit: an anterior and posterior rhinoscopy, oropharyngoscopy, laryngoscopy and thorough neck inspection and palpation, accompanied by an evaluation of the anthropometric data and the morphology of the facial skeleton – the latter aimed at referring the patient for a possible maxillofacial assessment.

RHINOSCOPY

Nasal involvement in OSAS is controversial, with several different studies both supporting and opposing such an association. It holds true, however, that inspection of the nasal cavities is an integral part of an ENT visit. It is indeed clear that nasal resistance may precipitate pharyngeal collapse, besides being among the possible causes of low compliance in both ventilation therapy (because of the increased pressures required due to the nasal stenosis) and surgical palatal therapy.

After a thorough examination aimed to detect a deviated septum, hypertrophic turbinates, polypoid masses, it can be useful to refer the patient for a thorough study of the nasal function by instrumental tests, such as: fiber rhinoscopy, rhinomanometry, acoustic rhinometry and mucociliary transport test.

OROPHARYNGOSCOPY

Oropharyngoscopy of OSAS patients deserves particular attention, as it targets directly the most often affected structures in this disorder. The otolaryngologist needs to focus on palatal structures, particularly the anatomy of the palatal arches, tonsillar fossa, uvula, palatal roof and the whole body of the tongue, searching for asymmetries, prolapses and muscle or mucous hypertrophies. Oropharyngoscopy standardization is achieved by using the Friedman-modified Mallampati score and is necessary in order to correlate the size of the tongue with the palate roof and the tonsil arches and, even more importantly, to assess the hypopharyngeal obstruction index, a measure correlated according to several authors to OSAS severity[7] (Figure 1). Likewise, a "tonsil grading" score is useful to quantify tonsil hypertrophy (Figure 2). For paediatric patients, it is also useful to grade adenoid hypertrophy according to the Cassano grading system[8].

FIBEROPTIC NASO-PHARYNGO-LARYNGOSCOPY

Diagnosis and therapy of OSAS require uncovering the site, extension and severity of the obstruction. Endoscopy is the only test returning these three parameters for evaluation; its role is fundamental in both the selection of surgical patients and any troubleshooting during surgical follow-up. Endoscopy is indeed universally deemed the fundamental test for diagnostic framing, with its scope now broadened by being performed in sedation – which enhances its diagnostic accuracy, as we shall see shortly.

Endoscopy is performed by means of either flexible or rigid endoscopes. The former, introduced by Hopkins in the 1950s, offers a superior image quality due to their higher luminosity, but their employ in OSAS diagnostics is regrettably limited to nasal examination, under contact anaesthesia with 10% xylocaine.

Flexible endoscopes are easier on the patient and allow the technician to more accurately appraise all OSAS-related regions of the upper airways. Furthermore, recently introduced high-definition flexible endoscopes (flexible telelaryngoscopes) have closed the gap in image quality. Endoscopic examination focuses

Figure 1 Modified Mallampati grade (MMP)

Grade 1: tonsils, pillars and soft palate are clearly visible.

Grade 2: uvula, pillars and upper pole are visible.

Grade 3: soft palate is partly visible; while tonsils, pillars and the uvula base are all invisible.

Grade 4: hard palate only is visible.

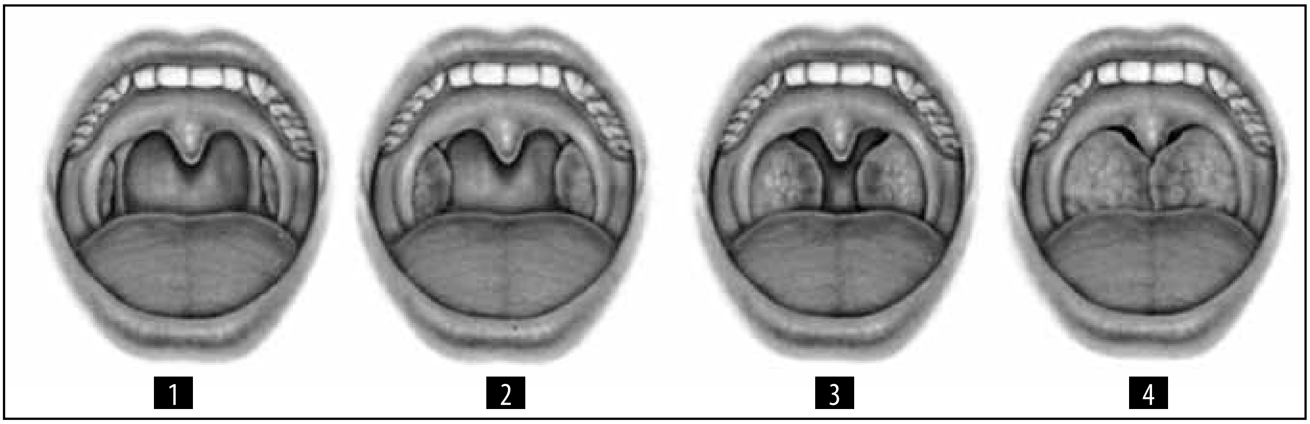


Figure 2 Tonsil size

Grade 1: tonsils are in tonsillar fossa, barely seen behind the anterior pillars.

Grade 2: tonsils are visible behind the anterior pillars.

Grade 3: tonsils are extended three quarters of the way to the mid-line.

Grade 4: tonsils are completely obstructing the airway.

first on the rhinopharynx and the upper soft palate, including its degree of proximity to the posterior wall of the pharynx. The uvula is to be examined next, appraising its size and any possible prolapse onto the tongue base. The tongue itself deserves attention, since lymphatic tissue hypertrophy, as well as true macroglossia, increases OSAS incidence[9]. The examination ends at the larynx-hypopharynx level, after evaluation of both the anatomy of the larynx (ptosic or "omega" epiglottis) and collapse-proneness of the lateral walls. To that end, the endoscopy needs to be performed with the patient subsequently seated and supine, in conditions of both nasal and oral breathing and through simulated snoring; likewise, Muller's manoeuvre needs to be performed in the attempt to locate any possible obstruction point by simulating dynamic, pharyngeal-laryngeal phenomena physiologically occurring during sleep due to the onset of negative pressures.

Muller's test was first introduced by Borowiecki and Sassani in 1983[10] and first standardized on the basis of the Sher[11] classification system, subsequently modified by Terris[12], who emphasised in particular the lateral collapse of the lateral pharyngeal walls; its advantages are easy execution, low invasiveness and a reproducible scoring hardly influenced by the test administrator.

Its role, however, is still very controversial, as several studies have shown its validity to be very limited, for the evaluation of the retro-lingual region for example[11,13,14], while other authors have stressed its value of successful prediction in case of UPPP to be limited to only 50% of cases[15].

There remains little doubt about the paramount importance of endoscopy in the evaluation of OSAS patients, as well as for their surgical suitability assessment, but frequent poor surgical outcomes have underscored the need to improve patient evaluation and selection. This has led several authors to introduce and steadfastly hone the "Sleep Nose Endoscopy" technique.

NASAL FUNCTIONAL TESTS

The relationship between nasal obstruction and respiratory disorders has been studied for more than 30 years. A close association has been hypothesized more than once between increased nasal resistance and severity of snoring, sleep apneas[16]. The link between nasal resistance and OSAS severity has been shown by several authors, but there are several contrasting studies which show no association, in their clinical trials, between nasal obstruction and apneas[17-19]. On the other hand, perusal of the literature does highlight that many patients affected by sleep-related respiratory disorders show symptoms of nasal obstruction; likewise, it is well known that an integral part of snoring-corrective surgery is nasal surgery. Besides, some authors suggest that a decrease in nasal resistance can be of use in CPAP ventilation therapy, due to the lower air pressures required[20].

The traditional otolaryngological approach to the nasal obstruction patient was made obsolete by the availability of modern diagnostic tools. Virtually all instances of nasal ailments can be resolved to their underlying causes and most appropriately treated by careful rhinological studies in specialized centres provided with adequate instrumentation. So, physical examination needs to be performed with optical endoscopes reaching areas of traditionally difficult accessibility, which allows an earlier and more detailed diagnose; afterwards, tests of nose function will be necessary for a correct diagnostic framing.

Basic tests of nose-sinus function, useful for the assessment of suspected OSAS patients, are measurements of the airflow and pressure within the nose made by active anterior rhinomanometry, acoustic rhinometry and mucociliary transport time (functional assessments of both the nasal fossae and their lining mucosa).

RHINOMANOMETRY

Rhinomanometry is an objective and non-invasive test of the nose respiratory function, measuring the airflow through the nasal cavities and the pressure this airflow exerts against them.

Data analysis outputs a sigmoid plot in a Cartesian axis system with P in the abscissa and V in the ordinate. Rhinometry can be either active or passive, relative to the nasal ventilation used to detect resistances. Active rhinomanometry (AR) is the most commonly used technique nowadays; it relies on the nasal ventilation performed by the patient during the test. An anterior (AAR) (Figure 3) or posterior setup (PAR) (Figure 4) is defined based on the location of the pressure sensor.

Rhinomanometry can be performed under a variety of conditions set in static, dynamic and functional tests. The standard procedure (static test) consists in baseline measurement in a seated patient. In our experience, normal values are <0.50 PA/cm^3/sec for unilateral resistance, and <0.25 for total resistance.

Functional tests include the nasal decongestion test (NDT), the valvular dilation test (VDT) and the nasal provocation test (specific and non-specific). Out of the dynamic tests, positional evaluation is worth mentioning as certainly necessary in case of suspected OSAS, since these patients often report a worsening of the nasal breathing when lying supine. The positional test prescribes a baseline AAR followed by a repetition of the rhinomanometric test, after having the patient lie supine for 30 minutes. The purpose of this test is to trigger a latent state of nasal dysfunction, evinced by an increased nasal resistance after prolonged lying in the supine position.

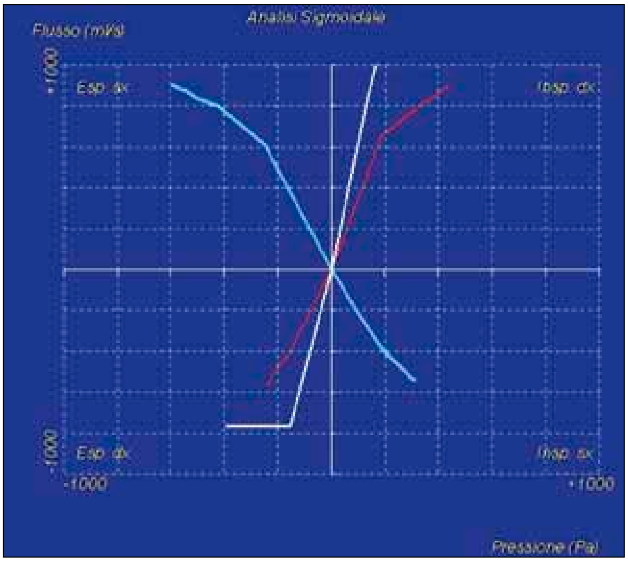


Figure 3 AAR - Anterior Active Rhinomanometry

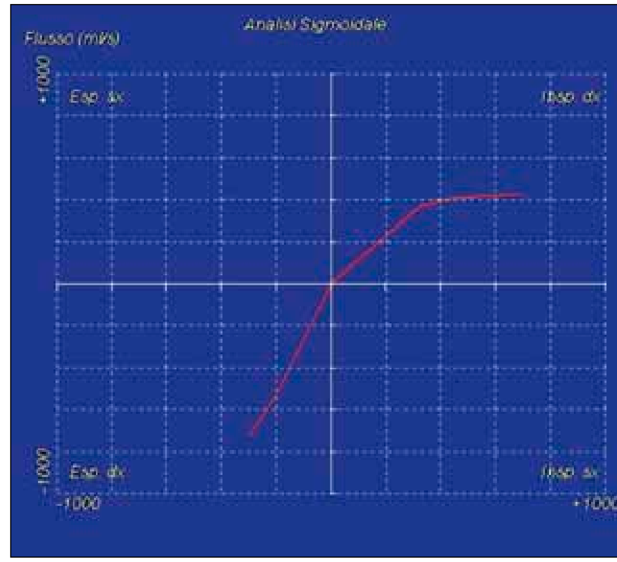


Figure 4 Posterior Active Rhinomanometry - PAR

NDT, performed in case of increased baseline resistance, prescribes the repetition of the rhinomanometry a short time after the administration of a low-latency nasal decongestant spray. The test is considered positive if resistance normalizes (functional stenosis), negative if it does not improve (structural stenosis). Thus, NDT is of notable clinical importance, swaying therapy choices toward either pharmacology or surgery.

VDT, indicated in case of suspected nasal valvular obstruction, is performed by rhinomanometric measurement after mechanical dilation of the nasal vestibule via nose strips. The test is positive if the nasal resistance decreases.

ACOUSTIC RHINOMETRY

Acoustic rhinometry is an instrumental test which geometrically measures the location of the nasal stenosis, by providing anatomical and structural data on the nasal cavities. First introduced by Hilberg in 1989[21], this technique can objectively assess the geometry of the nasal cavities and notably provide two-dimensional data about the transverse sections of each cavity, measured relative to nostril distance. Therefore, it can disclose and point out potential areas of obstruction and congestion.

An acoustic rhinometer gathers data from acoustic reflection and outputs the system impedance, which is inversely proportional to the transverse area, thus revealing the degree of nasal patency; by measuring the time it takes the sound waves to be reflected back to the origin, it is likewise possible to calculate the location of any nasal obstruction (Figure 5).

So, an acoustic rhinometer is made up of a sound wave generator producing sound stimuli in the audible range (150 – 10,000 Hz), sent up the nasal fossa as an acoustic click or periodic white noise, depending on the specific device used.

This sound is sent through a Bakelite tube, which does not interfere with acoustic propagation, connected at the end with an interchangeable nostril adapter, chosen on the basis of nostril size and side examined.

The test is to be performed during a gap in breathing, as sound propagation is affected by gas (air) density.

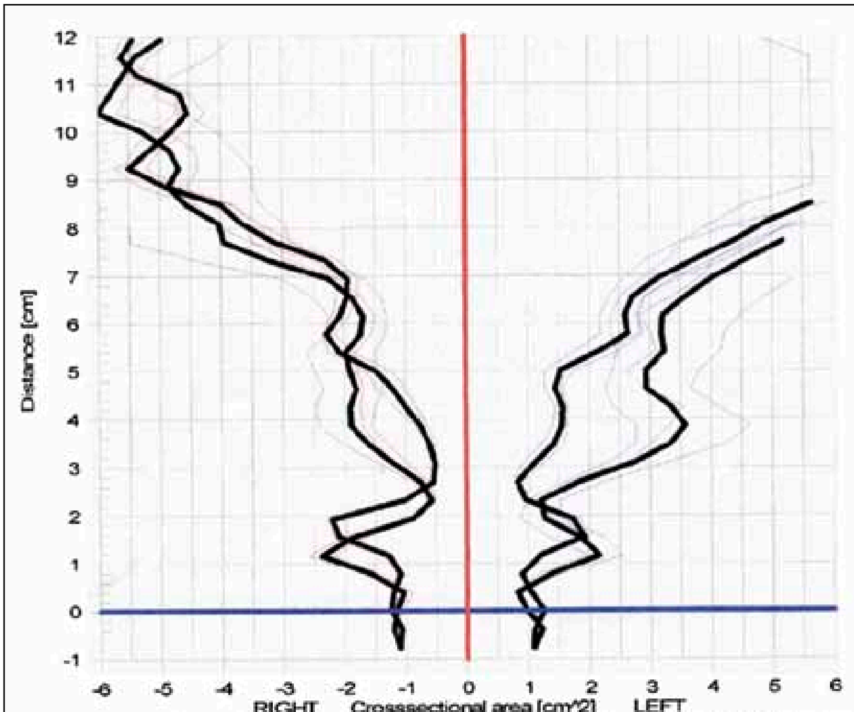
The choice and positioning of the nostril adapter is paramount, as it must not alter the structure of alar cartilages but at the same time be airtight. Indeed, our school has proposed to introduce a skull fixation mask (Passali et al., 1996)[22], with usage aimed to correctly position the head of the patient and make the test/retest conditions reproducible.

This is therefore an easily performed test, noninvasive, and requiring only minimal participation from the patient, being thus easily conducted even on children.

MUCOCILIARY TRANSPORT TIME

Mucociliary transport (MCT) is a physiological process referring to the flow of a film of mucus on top of the nasal epithelium (ciliated pseudostratified columnar epithelium). It is an important defensive mechanism against pathogenic noxae, clearing out any kind of foreign particle coming incessantly with inspired air.

MCT can be certainly appraised as an objective parameter of mucociliary function. Complex mechanisms are involved, making it a highly representative index of nasal mucosa state, anatomically as well as functionally.



Date and time	Side	Title	Dist	MCA1 VOL1		Dist	MCA2 VOL2 Nose Piece	
		Distance ranges:		[0.00:2.20] cm			[2.20:5.40] cm	
		Units:	[cm]	[cm^2]	[cm^3]	[cm]	[cm^2]	[cm^3]
2000-07-03 10:06:38	L	L 00-07-03 10:06:38	0.77	0.88	2.85	2.70	0.89	4.76
2000-07-03 10:07:08	L	L 00-07-03 10:07:08	0.77	0.94	2.97	2.70	0.74	3.84
2000-07-03 10:07:27	L	L 00-07-03 10:07:27	0.77	0.88	2.97	2.70	0.86	4.59
2000-07-03 10:07:56	L	Media basale	0.77	0.90	2.93	2.70	0.83	4.40
2000-07-03 11:05:39	L	L 00-07-03 11:05:39	0.39	0.89	3.68	2.31	1.52	11.31
2000-07-03 11:06:08	L	L 00-07-03 11:06:08	0.39	0.74	3.08	2.31	1.16	8.56
2000-07-03 11:07:15	L	L 00-07-03 11:07:15	0.39	0.85	2.77	2.20	0.95	7.15
2000-07-03 11:07:45	L	Media TDN	0.39	0.83	3.18	2.31	1.22	9.01

Figure 5 Acoustic Rhinometry

MCT study techniques make use of a tracer transported across the airways between two sites and involve measuring its transport time. MCT time (tMCT) is defined as the time elapsed since the deposition of the tracer onto the inferior turbinate head, until the tracer appears in the oropharynx. There are two types of tMCT measurement techniques: one making use of inert tracers detected by pharyngoscopy and one making use of radioactive tracers, revealed by a gamma camera.

In clinical practice, inert tracers are usually preferred, since chronological data are analogous to those provided by radioactive tracers, while costs are lower and execution easier. Moreover, possible biological harm by radiation from radioactive tracers should be taken into account, especially in those cases where many clinical checkups are mandatory.

The technique developed by our School involves the use of a mixture containing a known percentage of an insoluble substance (charcoal powder) and a soluble one (saccharine) (3%)[23]. Such a technique allows for the comprehensive study of the studied function, as the charcoal (besides being non-toxic and easily traceable, adhered as it is on the superficial nasal mucous film) is passively transported by mucociliary flow and provides a time more closely respondent to the MCT; on the other hand, saccharine diffuses into the gel-sol layer, thus allowing to obtain a time measurement closest to the physiological mucociliary clearance. So, the objective detection of charcoal, by direct pharyngoscopy, and the subjective detection of saccharine, by taste sensation, make a two-fold investigative technique.

SLEEP ENDOSCOPY

Much has been written for the last twenty years about nasal fiber endoscopy under sedation (sleep endoscopy). This technique was first described in 1991 by Croft and Pringle[24], who started out by observing that snoring and OSAS are dynamic phenomena mainly occurring in sleeping patients, and thought to visualize the obstruction sites of the upper airways during sleep phases.

In the original study, sleep was induced by short-acting benzodiazepines (midazolam). The fiber endoscope was well-tolerated by 95.8% of the study subjects and the obstructive problem was correctly identified in 79% of cases. Patients are made to lie supine on an operating table with low-intensity

Table 1
VOTE Classification according to de Vries et al.
(Shaded boxes reflect the fact that a specific structure-configuration cannot be seen)

Degree of obstruction:
0 No obstruction/vibration < del 50%
1 Partial obstruction/vibration >del 50%< del 75%
2 Complete Collapse
X Not visualized

Structure	Degree Of Obstruction	Configuration		
		A-P	Lateral	Concentric
Velum				
Oropharynx lateral walls				
Tongue Base				
Epiglottis				

Table 2
NOHL Classification according to Vicini et al. (This is associated with the pattern of collapse and Tonsil Size) Example: N3O4cTS3H2tLn

Site	Nose	Oropharynx	Hypopharynx	Larynx a) Supraglottic b) Glottic
Grade of Obstruction/ Collapse	Grade 1: 0-25%	Grade 1: 0-25%	Grade 1: 0-25%	Collapse present/absent
	Grade 2:25-50%	Grade 2:25-50%	Grade 2:25-50%	
	Grade 3: 50-75%	Grade 3: 50-75%	Grade 3: 50-75%	
	Grade 4: 75-100%	Grade 4: 75-100%	Grade 4: 75-100%	

lights. Throughout the procedure, oximetry and cardiac rhythms are accurately monitored, with supplemental oxygen delivered through a mask if necessary. Propofol is administered at an infusion rate of 50-75 mcg/kg/min in order to meet the target level of anaesthesia. At drug-induced sleep inception, the flexible fiber laryngoscope is introduced into the anesthetized nasal cavity and the examination (digitally recorded throughout) commences. During the examination, dynamic collapse needs to be evaluated at the level of the retro-palatal and retro-lingual regions, as well as of the laryngeal structures. The severity and the type (transverse, circular horizontal pattern) of the collapse need to be noted down for each region. For standardization purposes, several classification systems have been proposed to report severity, type and location of obstructions. The most commonly used at present are the VOTE classification (Table 1), introduced by de Vries[25], and the NOHL classification, introduced and standardized by the Italian School of Vicini[26] (Table 2).

To date, several modifications of such a technique have been published[27,28], with varying results. A recent literature review performed by Ravesloot and de Vries[29] on patients who underwent sleep endoscopy showed different regions of the upper airways collapse, such as the velopharynx, the oropharynx, the base of the tongue and the epiglottis, but it also underscored that the collapse is oftentimes multi-level. Furthermore, according to Rodriguez et al.[30], sleep endoscopy has evinced a high test-retest reliability compared to the other diagnostic techniques for OSAS.

CONCLUSIONS

A correct and complete diagnosis of OSAS is mandatory. The patients suspected of OSAS should undergo a basic set of tests for the gathering of clinical data followed by a more advanced clinical-instrumental investigation (ENT examination, fiberoptic naso-pharyngo-laryngoscopy, nasal functional tests - rhinomanometry or sleep endoscopy) in case of surgical planning.

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