ERJ Express. Published on April 8, 2010 as doi: 10.1183/09031936.00078009

Is tidal expiratory flow limitation predictive of sleep-related disorders in the elderly?

Guillot Maïlys [1,2], Costes Frédéric [2*], Sforza Emilia [2], Maudoux Delphine [2], Bertoletti Laurent [1], Barthélémy Jean-Claude [2], Roche Frédéric [2]
From:
1 Service de Pneumologie et d'Oncologie Thoracique, CHU St Etienne
2 Service de Physiologie Clinique et de l'Exercice, CHU St Etienne, Groupe Synapse

* corresponding author

Clinical trial registration: NCT00766584

Abstract

Sleep related disorders (SRD) represent an important health burden and their prevalence increases with age. In patients with snoring or sleepiness, the presence of expiratory flow limitation (EFL) using the Negative Expiratory Pressure (NEP) method is related to the Apnoea/Hypopnoea Index (AHI). In this study we examined whether EFL can be used to predict the obstructive sleep apnoea syndrome (OSAS) in healthy asymptomatic older subjects.

A group of 72-year old subjects (n=448, 44% males) with a mean BMI of 25.5±3.8 $kg.m^{-2}$ were examined. All subjects underwent spirometry, NEP (-5 cmH_2O, sitting position) and ventilatory polygraphy (VP).

Spirometry was within normal values in 88% of the group and EFL was present in 143 (32%) subjects with a higher prevalence in females (89/249 vs 54/199 in females and males respectively). VP showed an AHI<15/hours in 238 subjects (53%) and OSAS with an AHI≥15/h in 47%. EFL was found in 15% of subjects with OSAS. Consequently, EFL had low sensitivity and specificity in the prediction of OSAS (31.4% and 67.7%, respectively).

We conclude that the prevalence of expiratory flow limitation is elevated in healthy older subjects and cannot be used to predict the presence of sleep related disorders in an older population.

Words count: 199

Keywords: age, airflow limitation, obstructive sleep apnea

Short title: NEP and OSAS in elderly

Introduction

Sleep related disorders, and especially obstructive sleep apnoea syndrome (OSAS), represent a major public health problem. Its prevalence increases with age [1] and OSAS is associated with cardiovascular morbidity, which may be prevented by adequate diagnosis and treatment [2]. In a previous epidemiological examination study we found a high rate of unsuspected sleep-related disorders in a 65-year old healthy cohort [3]**.**

OSAS diagnosis relies on polysomnography (PSG), which is both cost- and time-consuming, and so is currently used only for symptomatic patients. Others screening methods are available. Pulse oximetry is only useful for screening night desaturation. Ventilatory Polygraphy (VP) represents an alternative method to PSG although it does not enable sleep architecture to be studied. VP is currently accepted as a valuable tool for screening.

Several studies have emphasized that upper airway (UA) collapsibility, one of the mechanisms responsible for OSAS, could be revealed with the negative expiratory pressure method (NEP), showing a transient decrease in expiratory flows provoked by the airway depression. From previous studies it was suggested that the presence of an expiratory flow limitation revealed by NEP could predict sleep apnea in selected patients but this relation has never been studied in a large group of asymptomatic subjects. The NEP technique consists in applying a negative pressure during expiration which increases the transpulmonary pressure and in turn the expiratory flow [4]. On the contrary, an expiratory flow limitation is evidenced by no change or a decrease of expiratory flow with NEP, which represents an extra or intra thoracic obstruction of the airways. Typical examples of flow/volume curve with NEP are given in figure 1.

Anatomical structures and neuromuscular control are implicated in the patency of the UA. They vary within the respiratory cycle, with sex and sleep state, leading to change in the cross sectional area of the UA. These parameters influence the UA closing pressure, which participates in the onset of apnea or hypopnea. The airway collapsibility seems to be more marked in older subjects due to decreased motor control of the UA and changes in the bony structures secondary to edentulism [5, 6]. The link between expiratory flow limitation (EFL) and OSAS has been demonstrated in snorers and symptomatic middle-aged patients [7-11]. De Bisschop et al. [12] found a high prevalence of EFL in elderly (up to 50% in females) in healthy subjects, which increases with age. This could be explained by the change in age-related thoracopulmonary mechanics, leading older subjects to breathe at a lower pulmonary volume. So the physiological reduction in expiratory flow in the elderly could reduce the

sensitivity and specificity of EFL used in the screening of OSAS. The question remains as to whether EFL could be predictive of sleep-related disorders in asymptomatic and older subjects.

The objectives of this study were therefore twofold: to confirm the high prevalence of EFL in the elderly and to answer the question whether EFL could be used as a screening method to diagnose OSAS.

Subjects and Methods

Subjects

The subjects enrolled in this study had already participated in our PROOF cohort study. Briefly, the subjects were recruited via the electoral rolls from amongst the inhabitants of the city of Saint Etienne and were assessed for autonomic nervous system activity, sleep-related disorders and the occurrence of cardiovascular events during a 7-year follow-up. The description of the primary end-points and the characteristics of the population have been published elsewhere [3].

During the last examination cycle (April 2006 – June 2008), when the subjects were then aged 72, we additionally investigated lung function and expiratory flow limitation using the NEP technique. We also measured body mass index and neck circumference. Sleepiness was categorised using the Epworth sleepiness scale; respiratory symptoms and smoking history were assessed by questionnaire.

In a subgroup of 26 subjects, we recorded VP, performed spirometry and NEP 2 years later. They were selected amongst severe OSAS (n=6) and OSAS- subjects (n=20).

The PROOF study was approved by our local ethics committee (CPP Rhône-Alpes Loire) and all subjects gave their written informed consent before participating.

Methods

Each subject underwent pulmonary function tests and ventilatory polygraphy (VP) on 2 consecutive days.

Lung function tests. Maximal flow/volume curves were performed in accordance with ERS recommendations, in a sitting position, and the best of 3 reproducible assays was recorded. The spirometer (Vmax SensorMedics, Yorba Linda, CA, USA) was calibrated with a 3-litre syringe before every series of measurements. All measurements were compared to predicted equations [13].

Expiratory flow limitation. EFL was investigated using the NEP technique (Hypair, Medisoft Dinan, Belgium) in the sitting position. In the additional group of 26 subjects, NEP was applied in both sitting and supine position. The expiratory flows were compared during spontaneous breathing and with NEP, applying a 5 cmH_2O depression at the mouth. The negative pressure was applied by a Venturi device connected to a pneumotachograph. The

principle of NEP is based on increase in pressure gradient between the alveoli and the mouth, which should increase expiratory flow in the absence of airflow limitation. The degree of flow limitation was assessed as the percentage of tidal volume where expiratory flows did not increase compared to the spontaneous breath [14]. This was automatically computed by the machine and was not modified by the investigators.

Tidal flow/volume curves were eliminated if they differed by more than 10% from the preceding spontaneous V_T. The average percentage of V_T flow-limited was calculated from 5 NEP V_T and EFL was retained when at least 20% of V_T was flow-limited (EFL+).

All measurements were performed by 3 investigators (MG, FC, LB), who were blind to the results of the sleep study.

Sleep study. Details of the ventilatory polygraphy (VP) system and the methodology used have been published elsewhere [15, 16]. Briefly, the VP (HypnoPTT, Tyco Healthcare, Puritan Bennett) recorded ECG tracings (one lead), pulse oxymetry (sampling rate: 1 Hz, minimal time duration to define an oxyhaemoglobin desaturation event: 10 sec), rib cage excursions (transthoracic impedance), body position and nasal pressure for measurement of ventilation. All the recordings were made overnight, at home, on the night before or after the in-hospital respiratory evaluation. A recording duration of at least five hours was required to validate the sleep study. All the recordings were validated visually and manually scored for apnoea/hypopnoea and UA high resistance events runs by blind investigators. Apnoea and hypopnoea events were defined according to previously published guidelines [17] and an oxyhaemoglobin desaturation threshold > 3% was chosen. The apnoea-hypopnoea index (number of apnoea and/or hypopnoea events per hour sleep: AHI), as well as the oxyhaemoglobin desaturation index (number of desaturations per hour in bed: ODI) were calculated. We also evaluated the mean SaO_2, the % of recording time below 90% and the minimal value recorded during sleep (Nadir SaO_2), as indices of nocturnal hypoxemia. Obstructive sleep apnea syndrome (OSAS) was retained when at least 50% of events were obstructive [18, 19]. In the same way, we separated the subjects according to the predominance of hypopneas (>50% of total events) or of apneas.

From previously reported data an obstructive AHI≥15 is considered to be diagnostic of the obstructive sleep apnoea syndrome in the elderly [20, 21]. Cases were defined as moderate or severe with an AHI between 15 and 30 or more than 30, respectively.

All sleep studies were analysed by the same investigator (FR).

Statistical analysis

Results are expressed as mean ± 1 standard deviation (± 1 SD). We compared anthropometric and spirometric values of the subjects with EFL (EFL+ or EFL-), and subjects with or without OSAS using unpaired Student *t* tests. The prevalence of EFL in different subgroups of subjects was compared by χ^2 (Fisher's exact test).

We calculated the sensitivity (Se), the specificity (Sp), the positive predictive value (PPV), the negative predictive value (NPV), the false positive (FP) and false negative (FN) rates of EFL for predicting OSAS using a threshold for AHI ≥15.

We next added high Epworth scale scores (>10) to EFL for predicting OSAS.

All the analyses were carried out using the Statview 5.0 software.

Results

A total of 448 subjects (250 females, 56%, and 198 males, 44%) were included. Their characteristics are given in Table 1. In general they were of normal weight: only 45 (10%) were obese (BMI>30 $kg.m^{-2}$) although this subset of subjects had similar BMI and neck circumference measurements to the rest of the study population.

The Epworth score was within normal ranges (5.0 ± 3.6 for females and 6.7 ± 3.8 for males) with 57 (12.7%) subjects considered as sleepy with an Epworth score of more than 10.

Spirometry and NEP results:

Spirometry was normal in 396 subjects (88%). 42 (9%) patients showed an obstructive pattern and a restrictive pattern was seen in 10 (2%).

$\%V_T$ flow-limited tended to be higher in females than in males (21.0±27.3% vs 16.3±26.7%, p=0.06). The presence or absence of bronchial obstruction did not influence the $\%V_T$ flow-limited (21.4±25.8% vs 18.2±27.0%, p=0.2).

Considering the 20% V_T flow-limited cut-off, EFL was present in 143 subjects (32%) and tended to be more frequent in females (62% vs 38%, p=0.05).

EFL was not correlated to BMI or neck circumference.

In the additional subgroup of 26 subjects spirometry was normal in all but two (obstructive pattern), and stable compared to the previous measurements. Results of VP were also unchanged (AHI>30, n=6, and AHI>15, n=20). In 7 subjects (26.9%), EFL was considered in supine position (54.5%V_T flow limited) while it was absent in sitting position. Among them

OSAS was present in only 2. So, the combination of EFL measurement in both supine and sitting position did not increase the predictive value of NEP for OSAS in this selected group of subjects.

Results of ventilatory polygraphy (table 1):

238 subjects (53%) had no OSAS (153 F and 83 M). 135 subjects (30%) had moderate OSAS (69 F and 66 M) and 75 subjects (17%) had an AHI≥30/h (26 F and 49 M).

All the subjects had an obstructive sleep apnea syndrome considering the predominance of obstructive events. In all but one eliminating central events did not change the AHI in a way that the diagnosis of the subjects was modified.

Among the subjects with an AHI≥15/h, only 25 (11.9%) were receiving treatment (hypnotics, muscle relaxants, morphine derivatives, anxiolytics) that may have altered upper airway tone and thus the NEP measurements.

EFL vs VP

When analyzing both the NEP and VP (data given in table 2) of the 143 EFL+ subjects, 77 (53.8%) were found to have an AHI<15, 41 (28.7%) were in the 15≤AHI<30 band and 25 (17.5%) subjects had an AHI≥30.

This gives a weak but non significant relationship as well as a poor predictive value: Se of 33% and 30% for AHI≥30 and 15≤AHI<30 respectively; PPV of 17.5% and 28.7%, for the presence of EFL in the detection of an OSAS (table 3).

Among the 305 EFL- subjects, 161 subjects (53%) had an AHI<15, and 144 subjects (32%) an AHI≥15. Sensitivity was improved but the positive predictive value remains low (table 3).

These statistical results did not vary with gender.

Most of the subjects were hypopneic considering the predominance of hypopneas (147/210, 70%, with 72 M and 97 F). Only 44 of them (29.9%) were EFL+ and this percentage was similar for men and women (27.8% and 24.8% respectively). The prevalence of EFL+ was similar in the hypopnea group compared to the apnea group (p=0.9).

Obstructive events were more frequent in dorsal than in lateral position (62.6% in males and 64.2% in females). However only 28.9% of the subjects in the dorsal subgroup were EFL+ (31.3% in M and 26.2% in F, p=0.09 and 0.9 respectively).

Considering the 57 sleepy subjects, 25 had an AHI<15 (43.9% of this subset) and 10 subjects had an AHI≥30 (17.5%). The Epworth Sleepiness Score was therefore not a good

predictor of OSAS; Se and PPV were low: 15.2% and 56.1% respectively for AHI≥15 and 13.3% and 17.5% for AHI≥30.

In order to assess whether the presence of clinical complaints such as sleepiness could be used to define the presence of sleep disordered breathing (SDB) we examine the 20 subjects having both an EFL and an Epworth score >10 (4.5% of the total and 9.5% of the OSAS subjects). Only 13 subjects had an AHI≥15, leading to very low Se and PPV (7.6 and 53.3%, respectively). Similar results were obtained in the 3 subjects with AHI≥30 (9.3 and 23.3% for Se and PPV respectively). Predictive value was not better for the 270 non-somnolent and EFL- subjects, of whom 143 had no OSAS.

Discussion

In this study, we did not find any relationship between the occurrence of expiratory flow limitation with NEP, performed in awaked subjects in seated position and with a 5 cmH_2O depression, and sleep related disorders in our population of older subjects, leading to the conclusion that NEP is not suitable for epidemiological screening of OSAS. However, we did confirm that the prevalence of EFL is elevated in elderly (one third of the subjects), especially in women.

Relationship between NEP and OSAS

The characteristics of our population corresponded to that of the usual population of this age range with more women than men and a similar sex ratio for the prevalence of OSAS [3].

Given the high prevalence of SRD we noted in this cohort, it seemed interesting to look for a relationship between SRD and EFL. Indeed, several studies have emphasized that the NEP technique was able to detect patients with OSAS by the visualization of a transient decrease in expiratory flow at the onset of negative pressure. This phenomenon was uncommon in the subjects of the present study. Moreover, we found a low predictive value of NEP to detect SRD.

Although one study found a limited usefulness of NEP to detect OSAS in a small group of apneic patients and snorers [22], others studies demonstrated a higher incidence of EFL with NEP [7-11, 23] in OSAS patients.

In a large sample of middle-aged patients with clinically suspected OSAS or with snoring, Van Meerhaeghe et al. [8] found a moderate sensitivity and specificity for predicting OSAS and the relationship between EFL and AHI was more significant in the supine than the sitting position. Using ROC analysis, these authors defined a cut off value of 27.5% of V_T flow-limited to predict an increase in AHI. In this study, we arbitrarily fixed a cut off value of 20%. It was chosen from our clinical experience which has demonstrated the inconstant presence of expiratory flow limitation at different NEP breaths below 20% V_T flow-limited. Nevertheless, reanalysing the data with a 27.5% cut off value for EFL did not improve the sensibility/specificity of the NEP technique. So, our definition of flow-limited subjects could not explain our negative results.

In most studies EFL was more common when the patients were studied in the supine than in the seated position. For practical reasons, it was not possible for us to explore EFL in both positions and we acknowledge that it is an important limitation in our study. However, in an

additional subgroup of 26 subjects explored with NEP in sitting and supine position, we found that considering EFL in supine position did not influence the prediction of OSAS. Although we can not draw definite conclusion with this small subgroup of subjects, this result suggest that the experimental conditions of EFL measurement could not solely explain the lack of prediction of OSAS by the NEP method.

Discrepancies between our study and previous reports

An increased occurrence of EFL has been reported in various studies [7, 10, 23] and it has been ascribed to upper airway collapsibility in OSAS patients. Several differences between these studies and ours could be mentioned. Firstly, they included patients attending a sleep clinic, thus with a clinical suspicion of OSAS or snorers. We can surmise therefore that these subjects had more severe or more long-lasting sleep disorders than those in our epidemiological study. Secondly, most of the patients included were younger than ours and were overweight or obese whereas only 10% of our subjects had a BMI >30 $kg.m^{-2}$. However, Baydur et al. [24] found that EFL was rare in obese patients and that its incidence was as common as in healthy controls. Thus the difference in weight can not explain the discrepancy between our results and those in previous studies.

The importance of EFL could be expressed in a more complex, and maybe in a more sensitive way than in our study. Tamisier et al. [9] calculated the area under the curve with NEP compared to the control condition and reported that a value of less than 160% and 180% for -5 and -10 cmH_2O respectively identified patients with OSAS. Alternatively, Rouatbi et al. [11] recorded oscillations on the flow/volume curve and their numbers increased significantly in OSAS patients and snorers. It seems rather difficult to quantify this in a clinical setting and to make the number of oscillations a suitable index for SRD detection.

Whatever the differences between our study and others, it appears unlikely that the absence of a relationship between EFL and SRD can be explained solely by technical or methodological reasons.

Limitation of our study

Type of the sleep events could have influenced the presence or not of EFL. NEP is supposed to increase the UA collapsibility, so we can suspect that EFL would be more closely correlated to hypopnea than to apnea. However our results do not support this since the percentage of expiratory flow limitation was similar according to the predominance of hypopneas or apneas, without any influence of gender.

UA stability also vary with the position of the subjects, the events being more frequent in dorsal than in lateral position. Although we confirm the predominance of events in dorsal

position, it did not influence the presence or not of EFL. These results suggest that the mechanism by which obstructive events occurred differ during sleep and during the application of NEP.

We did not control the position of the neck during the application of the NEP. Indeed, Walsh et al. [25] found that head flexion increased the pharyngeal critical closing pressure (Pcrit) and thus promoted the collapsibility of the upper airway. This could partly explain the high prevalence of EFL+ but not the difference between males and females.

Prevalence of EFL in elderly

We found an expiratory flow limitation in about a third of the subjects with a tendency to a higher prevalence in women. We can be confident in this result since the subjects in the Proof cohort were not selected on respiratory complaints. Moreover, subjects' characteristics of our subgroup of 448 subjects did not differ from those of the whole cohort (sex ratio, prevalence of EFL+ and OSAS, BMI, percentage of airway obstruction). We found that EFL was not influenced by the existence of respiratory symptoms evoking asthma or COPD, by the smoking habits, by the NYHA score or by the presence of obstruction of the airways assessed by FEV1/FVC < 0.7. These parameters cannot also explain the difference in prevalence of EFL with sex.

Surprisingly, we found a higher prevalence of EFL among males with a low Forced Vital Capacity (<80% predicted value on spirometry) but not in females. We confirm the results of De Bischop et al. concerning the elevated prevalence of EFL in elderly, especially in females, but we have no consistent explanation for the difference with sex. This deserves further study.

Physiopathology of OSAS in elderly

The presence of obstructive sleep apnoea is partly related to a greater Pcrit, which reflects the increase in UA collapsibility [26-28]. Eilkermann [29] showed that increasing age was correlated with both pharyngeal collapsibility and an increase in pharyngeal resistance during sleep. Ageing is characterized by increased Pcrit and UA resistance [28], predisposing the subject to facilitated upper airway closures. Thus the lack of correlation between an EFL under NEP and the presence of OSAS appears puzzling and suggests that factors other than UA collapsibility must also be responsible for the high prevalence of obstructive sleep apnoeas in the elderly. The absence of correlation between UA morphology measured by computed tomography and OSAS has been demonstrated by Mayer [30]. We extend this previous result, and demonstrate that in older subjects NEP is neither sensitive nor specific to explore the dynamic UA compliance.

The question remains as to why these subjects presented a high incidence of EFL when a low level of negative expiratory pressure was applied at the mouth. Our study was not designed to detect an increasing prevalence with age, as showed by De Bisschop et al. [12]. One cause could be facilitated UA collapse caused by slackening of the soft tissue with age, as has already been demonstrated with the decline in tongue strength [31]. A second cause could be that older subjects could breathe at a lower volume, close to the residual volume, and the tidal expiratory flows would encroache the maximal flow/volume loop. This change in ventilatory mechanic could explain airflow limitation with NEP; thus EFL with NEP would reflect an adaptative strategy for breathing and not a pathological pattern such as an upper airway collapse.

These physiological adaptations with age could explain why EFL with NEP present a so high negative predictive value in detecting OSAS. From the design and the aim of the study we could not assert that a low Functional Residual Capacity is associated with the presence of EFL and is predominant in women. Conditions during the night are obviously different from those present in our experimental conditions, which would explain why expiratory flow limitation during the day did not correspond to the occurrence of hypopneas/apneas.

Relationship between OSAS and sleepiness in elderly

The characteristics of the subjects studied here, for whom a diagnosis of severe OSAS (AHI≥30) was made for 17% of them, were usual for this age range with normal BMI values and low sleepiness scores. However 25 of the 75 OSAS subjects, including 16 females (64%), were on medication that could have influenced sleep or muscular tone (hypnotics, muscle relaxants, morphine derivatives, anxiolytics). However, even if we exclude these subjects, there is no difference in the statistical analyses for the 423 other subjects. Moreover, in accordance with previous studies, sleepiness evaluated with the Epworth sleepiness scale did not allow us to predict the existence of OSAS [1, 32-35]. Furthermore, the combination of OSAS, defined as AHI≥15, and the presence of sleepiness, did not increase the predictive values of the NEP.

Conclusion

In a large subset of older healthy subjects, a high incidence of sleep related disorders and expiratory flow limitation were detected using the NEP technique. However, the presence of EFL was not predictive of SRD and consequently NEP was not found to be suitable for epidemiological screening of OSAS.

Legend of figure

Figure 1.

Typical flow/volume curves obtained in 3 subjects of the study during spontaneous breathing and with: a/ no expiratory flow limitation. b/ extra-thoracic expiratory flow limitation, attested by an early decreased of the expiratory flow. c/ intra-thoracic expiratory flow limitation, attested by an end-expiratory decreased of the expiratory flow.

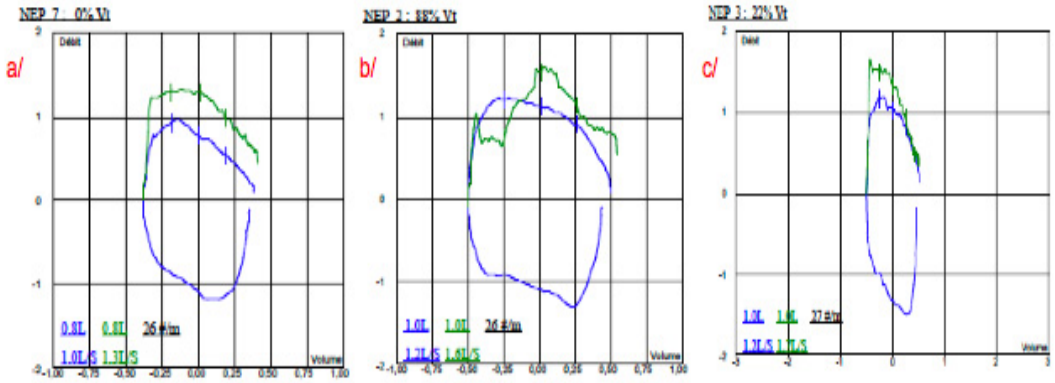

Table 1: Characteristics of the population with their results for spirometry and nocturnal ventilatory polygraphy (m±SD).

	All subjects	Males	Females
N (%)	448	199 (44.4)	249 (55.6)
Age (yrs)	72 ± 2	72 ± 1	72 ± 2
BMI (*kg.m^{-2}*)	25.5 ± 3.8	25.8 ± 3.2	25.2 ± 4.2
Neck circumference (*cm*)	36.8 ± 3.8	39.7 ± 3.0	34.5 ± 2.7
Epworth sleepiness score	5.7 ± 3.9	6.7 ± 3.8	5.0 ± 3.6
Pulmonary Function Tests			
FEV_1 (*% pred*)	102 ± 17.3	99.8 ± 17.8	103.8 ± 16.7
FVC (*% pred*)	108.8 ± 17.5	103.4 ± 16.5	113.0 ± 17.1
PEF (*% pred*)	98.3 ± 20.6	103.7 ± 21.8	93.9 ± 18.4
FEF_{25-75} (*% pre)d*	71.2 ± 26.3	74.4 ± 27.3	68.5 ± 25.3
Ventilatory polygraphy results			
Total sleep time *(min)*	442.1 ± 111.4	424.4 ± 115.8	456.2 ± 105.8
Average SO_2 *(%)*	95.3 ± 1.6	95.4 ± 1.6	95.2 ± 1.5
Minimum SO_2 *(%)*	89.3 ± 4.4	89.0 ± 4.6	90.0 ± 4.2
ODI *(n/h)*	9.7 ± 9.7	12.3 ± 11.3	7.7 ± 7.8
AHI *(n/h)*	17.7 ± 14.3	21.6 ± 15.6	14.6 ± 12.3
IA > IH *(n, %)*	63 (30%)	41 (19.5%)	22 (10.5%)
Dorsal events *n (%)*	128 (63.4%)	67 (62.6%)	61 (64.2%)

ODI: Oxyhemoglobin Desaturation Index retained as a 3% decreased in SpO_2; AHI: Apnea Hypopnea Index recorded with ventilatory polygraphy; IA>IH: Apnea Index superior to Hypopnea Index; Dorsal events: number of subjects presenting a majority of events (>50% of total events) in dorsal position compared to lateral one.

Table 2. Presence of expiratory flow limitation in relation to the Apnoea/Hypopnoea Index. EFL (EFL+) was retained when at least 20% of V_T was flow-limited

	All subjects		Males		Females	
	EFL+ *n (% of all subjects)*	EFL- *n (% of all subjects)*	EFL+ *n (% of M)*	EFL-	EFL+ *n (% of F)*	EFL-
AHI<15	77 (17.2%)	161 (35.9%)	20 (10.1%)	64	57 (22.9%)	97
15≤ AHI <30	41 (9.2%)	94 (21.0%)	16 (8.0%)	50	25 (10.0%)	44
AHI ≥30	25 (5.6%)	50 (11.2%)	18 (9.0%)	31	7 (2.8%)	19

Table 3. Prediction of OSAS from EFL

	AHI<15	AHI≥15	15≤AHI<30	AHI≥30
Se	67.7	31.4	30.4	33.3
Sp	31.4	67.7	67.2	68.4
PPV	52.8	46.2	28.7	17.5
NPV	46.2	52.8	69.2	83.6
FP	47.2	53.9	71.3	82.5
FN	53.9	47.2	31	16.4

Se: sensitivity ; Sp: specificity ; PPV: positive predictive value ; NPV: negative predictive value ; FP: false positive ; FN: false negative

References

1. Duran, J., S. Esnaola, R. Rubio, and A. Iztueta, Obstructive sleep apnea-hypopnea and related clinical features in a population-based sample of subjects aged 30 to 70 yr. Am J Respir Crit Care Med, 2001. **163**(3 Pt 1): p. 685-9.
2. Marin, J.M., S.J. Carrizo, E. Vicente, and A.G. Agusti, Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: an observational study. Lancet, 2005. **365**(9464): p. 1046-53.
3. Barthelemy, J.C., V. Pichot, V. Dauphinot, S. Celle, B. Laurent, A. Garcin, D. Maudoux, J. Kerleroux, J.R. Lacour, M. Kossovsky, J.M. Gaspoz, and F. Roche, Autonomic nervous system activity and decline as prognostic indicators of cardiovascular and cerebrovascular events: the 'PROOF' Study. Study design and population sample. Associations with sleep-related breathing disorders: the 'SYNAPSE' Study. Neuroepidemiology, 2007. **29**(1-2): p. 18-28.
4. Koulouris, N., P. Valta, A. Lavoie, C. Corbeil, M. Chasse, J. Braidy, and J. Milic-Emili, A simple method to detect expiratory flow limitation during spontneous breathing. The European Respiratory Journal, 1995. **8**: p. 306-313.
5. Pack, A.I., D.A. Silage, R.P. Millman, H. Knight, E.T. Shore, and D.C. Chung, Spectral analysis of ventilation in elderly subjects awake and asleep. J Appl Physiol, 1988. **64**(3): p. 1257-67.
6. Riha, R.L., P. Brander, M. Vennelle, and N.J. Douglas, A cephalometric comparison of patients with the sleep apnea/hypopnea syndrome and their siblings. Sleep, 2005. **28**(3): p. 315-20.
7. Tantucci, C., A. Duguet, A. Ferretti, S. Mehiri, I. Arnulf, M. Zelter, T. Similowski, J.P. Derenne, and J. Milic-Emili, Effect of negative expiratory pressure on respiratory system flow resistance in awake snorers and nonsnorers. J Appl Physiol, 1999. **87**(3): p. 969-76.
8. Van Meerhaeghe, A., P. Delpire, P. Stenuit, and M. Kerkhofs, Operating characteristics of the negative expiratory pressure technique in predicting obstructive sleep apnoea syndrome in snoring patients. Thorax, 2004. **59**(10): p. 883-8.
9. Tamisier, R., B. Wuyam, I. Nicolle, J.L. Pepin, O. Orliaguet, C.P. Perrin, and P. Levy, Awake flow limitation with negative expiratory pressure in sleep disordered breathing. Sleep Med, 2005. **6**(3): p. 205-13.
10. Verin, E., C. Tardif, F. Portier, T. Similowski, P. Pasquis, and J.F. Muir, Evidence for expiratory flow limitation of extrathoracic origin in patients with obstructive sleep apnoea. Thorax, 2002. **57**(5): p. 423-8.
11. Rouatbi, S., Z. Tabka, M. Dogui, A. Abdelghani, and H. Guenard, Negative Expiratory Pressure (NEP) Parameters Can Predict Obstructive Sleep Apnea Syndrome in Snoring Patients. Lung, 2009. **187**(1): p. 23-8.
12. de Bisschop, C., M.L. Marty, J.F. Tessier, P. Barberger-Gateau, J.F. Dartigues, and H. Guenard, Expiratory flow limitation and obstruction in the elderly. Eur Respir J, 2005. **26**(4): p. 594-601.
13. Quanjer, P.H., Standardized lung function testing, ECSC 1993 update. The European Respiratory Journal, 1993. **6**(S16): p. 5-40.
14. Calverley, P.M. and N.G. Koulouris, Flow limitation and dynamic hyperinflation: key concepts in modern respiratory physiology. Eur Respir J, 2005. **25**(1): p. 186-99.
15. Ancoli-Israel, S., D.F. Kripke, W. Mason, and S. Messin, Comparisons of home sleep recordings and polysomnograms in older adults with sleep disorders. Sleep, 1981. **4**(3): p. 283-91.

16. Series, F. and I. Marc, Nasal pressure recording in the diagnosis of sleep apnoea hypopnoea syndrome. Thorax, 1999. **54**(6): p. 506-10.
17. Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. Sleep Med, 1999. **22**: p. 667-689.
18. Eckert, D., A. Jordan, P. Merchia, and A. Malhotra, Central sleep apnea: Pathophysiology and treatment. Chest, 2007. **131**(2): p. 595-607.
19. Yumino, D. and T. Bradley, Central sleep apnea and Cheyne-Stokes respiration. Proceedings of the American Thoracic Society, 2008. **5**(2): p. 226-236.
20. Mant, A., N. Saunders, and E. Eyland, Sleep habits and sleep related respiratory disturbance in an older population. Sleep '88, ed. H.J.e. al. 1989, Stuttgart: Gustav Fischer Verlag. 260-261.
21. International classification of sleep disorders, Ed.2: diagnostic and coding manual. Sleep Med, 2005.
22. Ferretti, A., P. Giampiccolo, S. Redolfi, S. Mondini, A. Cirignotta, A. Cavalli, and C. Tantucci, Upper airway dynamics during negative expiratory pressure in apneic and non-apneic awake snorers. Respir Res, 2006. **30**(7): p. 54.
23. Liistro, G., C. Veriter, M. Dury, G. Aubert, and D. Stanescu, Expiratory flow limitation in awake sleep-disordered breathing subjects. Eur Respir J, 1999. **14**(1): p. 185-90.
24. Baydur, A., L. Wilkinson, R. Mehdian, B. Bains, and J. Milic-Emili, Extrathoracic expiratory flow limitation in obesity and obstructive and restrictive disorders: effects of increasing negative expiratory pressure. Chest, 2004. **125**(1): p. 98-105.
25. Walsh, W., J. H., K.J. Maddison, P.R. Platt, D.R. Hillman, and P.R. Eastwood, Influence of head extension, flexion, and rotation on collapsibility of the passive upper airway. Sleep, 2008. **31**(10): p. 1440-7.
26. Sforza, E., C. Petiau, T. Weiss, A. Thibault, and J. Krieger, Pharyngeal critical pressure in patients with obstructive sleep apnea syndrome. Clinical implications. Am J Respir Crit Care Med, 1999. **159**(1): p. 149-57.
27. Boudewyns, A., N. Punjabi, P.H. Van de Heyning, W.A. De Backer, C.P. O'Donnell, H. Schneider, P.L. Smith, and A.R. Schwartz, Abbreviated method for assessing upper airway function in obstructive sleep apnea. Chest, 2000. **118**(4): p. 1031-41.
28. Kirkness, J.P., A.R. Schwartz, H. Schneider, N.M. Punjabi, J.J. Maly, A.M. Laffan, B.M. McGinley, T. Magnuson, M. Schweitzer, P.L. Smith, and S.P. Patil, Contribution of male sex, age, and obesity to mechanical instability of the upper airway during sleep. J Appl Physiol, 2008. **104**(6): p. 1618-24.
29. Eikermann, M., A.S. Jordan, N.L. Chamberlin, S. Gautam, A. Wellman, Y.L. Lo, D.P. White, and A. Malhotra, The influence of aging on pharyngeal collapsibility during sleep. Chest, 2007. **131**(6): p. 1702-9.
30. Mayer, P., J. Pépin, G. Bettega, D. Veale, G. Ferretti, C. Deschaux, and P. Lévy, Relationship between body mass index, age and upper airway measurements in snorers and sleep apnoea patients. Eur Respir J, 1996. **9**: p. 1801-1809.
31. Crow, H.C. and J.A. Ship, Tongue strength and endurance in different aged individuals. J Gerontol A Biol Sci Med Sci, 1996. **51**(5): p. M247-50.
32. Rosenthal, L.D. and D.C. Dolan, The Epworth sleepiness scale in the identification of obstructive sleep apnea. J Nerv Ment Dis, 2008. **196**(5): p. 429-31.
33. Roure, N., S. Gomez, O. Mediano, J. Duran, L. Pena Mde, F. Capote, J. Teran, J.F. Masa, M.L. Alonso, J. Corral, A. Sanchez-Armengod, C. Martinez, A. Barcelo, D. Gozal, J.M. Marin, and F. Barbe, Daytime sleepiness and polysomnography in obstructive sleep apnea patients. Sleep Med, 2008. **9**(7): p. 727-31.

34. Hayashida, K., Y. Inoue, S. Chiba, T. Yagi, M. Urashima, Y. Honda, and H. Itoh, Factors influencing subjective sleepiness in patients with obstructive sleep apnea syndrome. Psychiatry Clin Neurosci, 2007. **61**(5): p. 558-63.
35. Mediano, O., A. Barcelo, M. de la Pena, D. Gozal, A. Agusti, and F. Barbe, Daytime sleepiness and polysomnographic variables in sleep apnoea patients. Eur Respir J, 2007. **30**(1): p. 110-13.