

## Indices from flow-volume curves in relation to cephalometric, ENT— and sleep—O<sub>2</sub> saturation variables in snorers with and without obstructive sleep-apnoea

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**ABSTRACT:** In a group of 37 heavy snorers with obstructive sleep apnoea (OSA, Group 1) and a group of 23 heavy snorers without OSA (Group 2) cephalometric indices, ENT indices related to upper airway collapsibility, and nocturnal O<sub>2</sub> desaturation indices were related to variables from maximal expiratory and inspiratory flow-volume (MEFV and MIFV) curves.

The cephalometric indices used were the length and diameter of the soft palate (spl and spd), the shortest distance between the mandibular plane and the hyoid bone (mph) and the posterior airway space (pas). Collapsibility of the upper airways was observed at the level of the tongue base and soft palate by fibroscopy during a Müller manoeuvre (mtb and msp) and ranked on a five point scale. Sleep indices measured were the mean number of oxygen desaturations of more than 3% per hour preceded by an apnoea or hypopnoea of more than 10 s (desaturation index), maximal sleep oxygen desaturation, baseline arterial oxygen saturation (Sa<sub>o</sub><sub>2</sub>) and, in the OSA group, percentage of sleep time with Sa<sub>o</sub><sub>2</sub> <90%. The variables obtained from the flow-volume curves were the forced vital capacity (FVC), forced expiratory and inspiratory volume in 1 s (FEV<sub>1</sub> and FIV<sub>1</sub>), peak expiratory and peak inspiratory flows (PEF and PIF), and maximal flow after expiring 50% of the FVC (MEF<sub>50</sub>).

The mean of the flow-volume variables, influenced by upper airway aperture (PEF, FIV<sub>1</sub>) was significantly greater than predicted. A significant correlation between flow-volume variables and the other indices was found only for FIV<sub>1</sub> (% pred), PEF (% pred) and for PIF with the maximal O<sub>2</sub> desaturation ( $r=-0.60$ ,  $r=-0.46$ , and  $r=-0.48$ , respectively) in the OSA group only.

We hypothesize that compensatory mechanisms, which increase the upper airway aperture during wakefulness, account for the raised PEF, and FIV<sub>1</sub>. The decrease of PIF, PEF and FIV<sub>1</sub>, variables related to upper airway aperture, with maximal O<sub>2</sub> desaturation can be explained by the mechanisms relating sleep O<sub>2</sub> desaturation, chemical control of tonic upper airway muscle activity, and upper airway aperture in OSA. *Eur Respir J., 1995, 8, 801–806.*

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The obstructive sleep apnoea syndrome (OSA) is characterized by an interplay of mechanical and neuromuscular factors. It was found that cephalometric radiographs of patients with OSA, if compared with controls, generally showed deviations in one or more of the following indices: the distance from the mandibular plane to the hyoid bone (mph), the posterior airway space at the level of the tongue base (pas), and the length and diameter of the soft palate (spl, spd) [1–8]. This led PARTINEN *et al.* [6], among others, to the conclusion that cephalometric roentgenograms can be useful in the diagnosis of OSA patients.

During sleep, the integrity of the pharyngeal airway is disturbed by a decreased chemosensitivity of the tonic activity of the upper airway muscles [9], leading to an enhanced

collapsibility in the inspiratory phase. Mathematical model-based studies, in which these mechanisms were incorporated, were able to simulate periodic apnoea intervals [10].

Up to now, maximal inspiratory and expiratory flow-volume (MIFV and MEFV) curves have shown no diagnostic value in differentiating snorers and OSA patients from controls [1, 11]. Indices from those curves, or the presence of sawtooth-like disturbances showed a high specificity but a low sensitivity. However, earlier investigations, performed during wakefulness, have shown a decrease of peak expiratory flow (PEF) and indices from the inspiratory part (peak inspiratory flow (PIF); forced inspiratory volume in 1 s, (FIV<sub>1</sub>)) in the presence of an increased extrathoracic upper airway resistance [12–15].

Our study was aimed at a further evaluation of the variables from MIFV and MEFV curves in relation to sleep O<sub>2</sub> desaturation and cephalometric indices in a group of snorers, with and without OSA. Moreover, estimates for the amount of upper airway collapsibility in the awake state and, in a subgroup, ventilatory response to CO<sub>2</sub>, were also obtained. The results will be discussed in terms of the mechanisms determining OSA.

## Material and methods

### Patients

The patient population consisted of 60 consecutive patients, admitted to our hospital for excessive snoring, irrespective of a history of nocturnal apnoeas or daytime sleepiness. Only patients without concomitant pathology of other origin entered the study. A standard questionnaire was used to reveal, among other things, daytime sleepiness and smoking. Anthropometric data are presented in table 1.

Table 1. – Anthropometric, sleep oxygen desaturation, flow-volume, ENT and cephalometric variables of the 60 snorers

Variable	Group 1 OSA (n=37)	Group 2 without OSA (n=23)
Sex M/F	35/2	18/5
Age yrs	51 (9)	45 (13)
BMI kg·m <sup>-2</sup>	29.5 (5.0)*	25.9 (3.5)
Baseline Sa <sub>o</sub> <sub>2</sub> %	95 (2)	94 (2)
Max. desat. %	12 (8)*	5 (4)
DI episode·h <sup>-1</sup>	21.1 (19.2)*	2.0 (1.3)
FEV <sub>1</sub> % pred	101 (14)	107 (10)
FVC % pred	107 (16)	111 (8)
PEF % pred	118 (23)	117 (20)
FIV <sub>1</sub> % pred	119 (18)	123 (10)
PIF L·s <sup>-1</sup>	6.7 (1.7)	7.3 (2.6)
MEF <sub>50</sub> % pred	88 (30)	92 (26)
m <sub>sp</sub>	2.8 (1.3)	2.6 (1.4)
m <sub>tb</sub>	1.0 (1.3)*	0.4 (0.7)
s <sub>pd</sub> mm	11.8 (1.6)	11.1 (2.0)
s <sub>pl</sub> mm	39.7 (5.9)	36.6 (7.0)
m <sub>ph</sub> mm	22.4 (7.5)	22.4 (6.8)
p <sub>as</sub> mm	11.6 (3.5)	11.7 (3.5)

Data are presented as mean, and SD in parenthesis. M: male; F: female; OSA: obstructive sleep apnoea; max. desat.: maximal oxygen desaturation; FEV<sub>1</sub>: forced expiratory volume in one second; FVC: forced vital capacity; PEF: peak expiratory flow; FIV<sub>1</sub>: forced inspiratory volume in one second; PIF: peak inspiratory flow; MEF<sub>50</sub>: maximal expiratory flow after expiring 50% of the FVC; BMI: body mass index; DI: desaturation index; m<sub>sp</sub> and m<sub>tb</sub>: ranking of collapsibility during Müller manoeuvre at the level of soft palate and tongue base, respectively; s<sub>pd</sub>: diameter of soft palate; s<sub>pl</sub>: length of soft palate; m<sub>ph</sub>: shortest distance between the mandibular plane and the hyoid bone; p<sub>as</sub>: posterior airway space. Significant differences between the groups are indicated by an asterisk; significance levels are denoted in the text.

### Cephalometric analysis

Standardized lateral skull radiographs were made during slow inspiration through the nose with the mandible and head held in a fixed position. The control of head posture was achieved by ear plugs and a specially designed frame. From the measurements determining facial morphology [1–8], four were chosen: length and diameter of the soft palate (s<sub>pl</sub> and s<sub>pd</sub>); shortest distance between the mandibular plane and the hyoid bone (m<sub>ph</sub>); and the posterior airway space (p<sub>as</sub>), defined as the minimal distance between the base of the tongue and the posterior pharyngeal wall. All patients showed an overall skeletal type.

### Ear, nose and throat (ENT) analysis

Under fibroscopic control of the upper airway, a maximal negative pressure effort with occluded mouthway (Müller manoeuvre) was performed. Collapsibility of the upper airways at the level of the base of the tongue (Müller tongue base (m<sub>tb</sub>)) and soft palate (Müller soft palate (m<sub>sp</sub>)) was assessed and ranked on a five point scale, ranging from 0 (no collapsibility of the airways) to 4 (complete collapse of the airways) in steps of 25% of the initial diameter.

### Polysomnography

During an overnight stay at the hospital, a sleep recording was made including: electroencephalography (EEG), electro-oculogram (EOG), and electromyography of the chin muscle for identification of sleep stages; abdominal and thoracic movements by impedance plethysmography; airflow at nose and mouth by thermistors; and transcutaneous oxygen saturation (Biox ear oximeter) to evaluate breathing. Apnoeas were considered as either obstructive, central or of the mixed type. In our statistical analyses, we used the desaturation index (DI), being the mean number of apnoeas or hypopnoeas per hour with a duration longer than 10 s, leading to an oxygen desaturation greater than 3%. On the basis of the desaturation index, patients were divided into two groups: snorers with OSA (Group 1) with a DI of >5 events·h<sup>-1</sup> sleep; and snorers without OSA (Group 2). In addition, baseline Sa<sub>o</sub><sub>2</sub>, maximal nocturnal oxygen desaturation and in Group 1, percentage of sleep time with Sa<sub>o</sub><sub>2</sub> <90% was measured.

### MEFV and MIFV curves

MEFV and MIFV curves were obtained with a heated pneumotachometer (Jaeger, Germany), which was volume-calibrated before each measurement. From at least three acceptable manoeuvres, (forced vital capacities (FVC) not differing more than 5%) the following variables were derived: FVC, PEF, forced expiratory volume in one second (FEV<sub>1</sub>), PIF and FIV<sub>1</sub> as maximal values. The maximal expiratory flow after expiring 50% of the FVC (MEF<sub>50</sub>) was taken from the curve with the highest FVC. FVC, FEV<sub>1</sub>, FIV<sub>1</sub>, MEF<sub>50</sub> and PEF were expressed as % predicted [16]. For PIF the absolute values were taken.

### Ventilatory CO<sub>2</sub> response

In a subgroup (n=11) the ventilatory CO<sub>2</sub> response (CO<sub>2</sub> sensitivity (SCO<sub>2</sub>)) was determined with a recently described quasi-steady-state ramp method [17]. During this measurement, end-tidal carbon dioxide tension (P<sub>ET,CO<sub>2</sub></sub>) was increased by about 0.25 kPa·min<sup>-1</sup> in a rampwise fashion, and mean increase in minute volume (V'<sub>E</sub>) and P<sub>ET,CO<sub>2</sub></sub> from the fifth until the eighth minute yielded the CO<sub>2</sub> sensitivity in L·min<sup>-1</sup>·kPa<sup>-1</sup>. The data were compared with reference values [18].

### Data analysis and statistics

For Group 1 (snorers with OSA) and Group 2 (snorers without OSA) mean values were obtained for the sleep oxygen desaturation data, body mass index (BMI) defined as weight (kg) per height squared (m<sup>2</sup>) and cephalometric, ENT and flow-volume indices.

Group means were compared by a nonparametric test (Mann-Whitney U-test). Comparisons with predicted were made with a Student's t-test. The BMI predicted was taken from SIMOPOULOS and van ITALIE [19]. Spearman rank correlations were obtained for the pulmonary function indices expressed in % predicted with respect to the cephalometric, ENT and sleep oxygen desaturation data. Taking the Bonferroni correction for multiple correlations into account, a value of p less than 0.005 was considered significant.

## Results

The group mean data, concerning anthropometric, flow-volume, ENT and cephalometric variables are presented in table 1, for the snorers with and without OSA. If a normal BMI of 25 kg·m<sup>-2</sup> is assumed [19], the patients with OSA appear significantly overweight compared both to normal subjects (p<0.005) and to the patients without OSA (p<0.005). Nineteen patients in the OSA group and 14 patients in the non-OSA group were regular smokers, this difference between the groups being nonsignificant.

From a randomly selected subgroup of 10 patients, in nine of them four, and in one of them three, MEFV/MIFV curves had to be obtained in order to meet the criterion of less than 5% difference between three FVC values. The mean variation coefficients and their standard deviations for the individual values of FIV<sub>1</sub>, PEF and PIF were, 2.4 (1.7), 6.4 (4.6) and 5.3 (3.3) %, respectively. They were not different from values in other investigations [20], and indicated the reliability of the maximum of the three individual values as representative index. In order to normalize for sex, age and height, values were expressed in percentage of predicted, except for PIF, for which no reliable reference data are available.

The flow-volume variables showed no significant differences between the two groups. Within the groups, the mean values for PEF and FIV<sub>1</sub> in both groups and FEV<sub>1</sub> and FVC in Group 2 were, however, significantly increased with respect to predicted (p<0.001). Marked

oscillations on the flow-volume curves were found in five patients from the OSA group and three from the group without OSA.

The mean (±SD) ventilatory response for CO<sub>2</sub>, measured at random in 11 patients (six with OSA and five without) was 15.0 (±5.3) L·min<sup>-1</sup>·kPa<sup>-1</sup> (range 8.3–25.5 L·min<sup>-1</sup>·kPa<sup>-1</sup>) which did not differ from reference, being 15.0 (±3.0) L·min<sup>-1</sup>·kPa<sup>-1</sup> [18].

Although the collapsibility at the level of the tongue base and at the level of the soft palate (mtb and msp) were both higher in the OSA group, only the difference between the mtb indices was just significant (p<0.05; t-test for group differences). No significant differences were found between the cephalometric variables in both groups.

For the OSA group, we found a large range for the percentage of sleep time with Sa<sub>a,O<sub>2</sub></sub> <90% (0.03–100% in a patient with 90% baseline Sa<sub>a,O<sub>2</sub></sub>; median value was 2.1%). Baseline Sa<sub>a,O<sub>2</sub></sub> was significantly correlated with

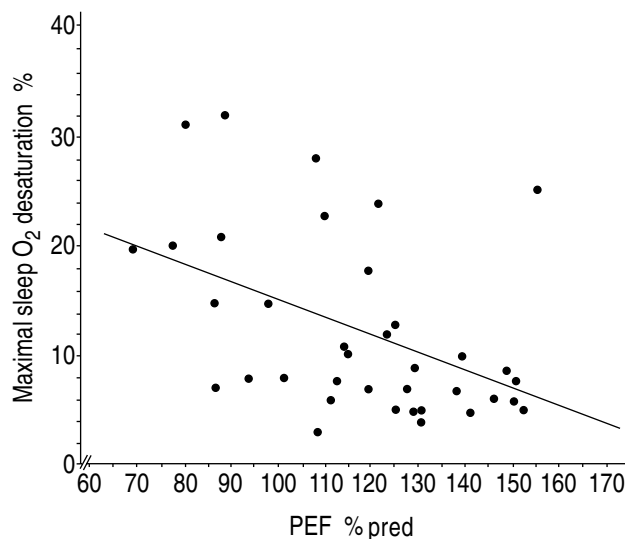


Fig. 1. — Maximal sleep O<sub>2</sub> desaturation presented against peak expiratory flow (PEF) in % predicted in the obstructive sleep apnoea (OSA) patients. Spearman's rank correlation:  $r = -0.46$ ;  $p = 0.005$ .

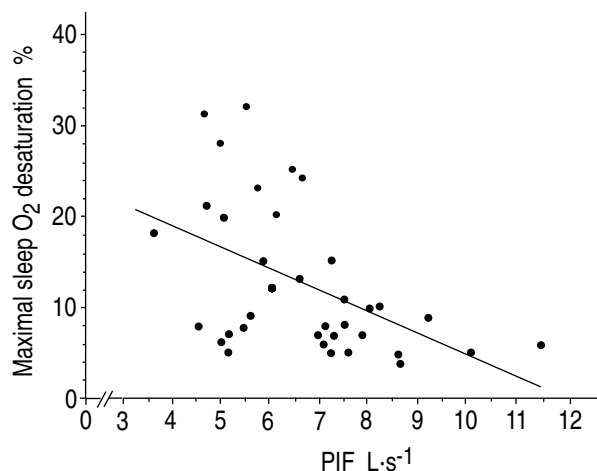


Fig. 2. — Maximal sleep O<sub>2</sub> desaturation presented against peak inspiratory flow (PIF) in the obstructive sleep apnoea (OSA) patients. Spearman's rank correlation:  $r = -0.48$ ;  $p = 0.004$ .

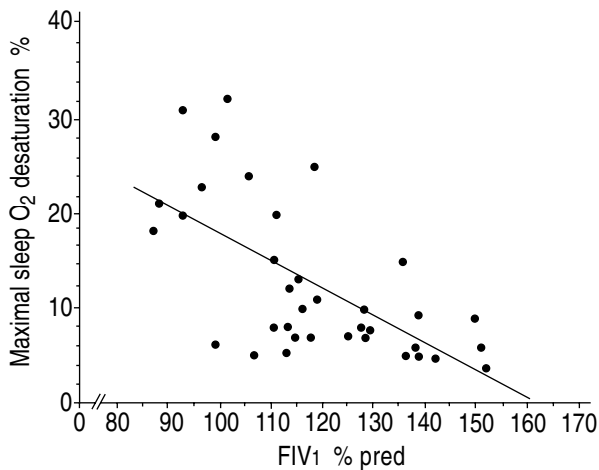


Fig. 3. — Maximal sleep  $O_2$  desaturation presented against forced inspiratory volume in one second FIV1 in % predicted in the obstructive sleep apnoea (OSA) patients. Spearman's rank correlation:  $r = -0.60$ ;  $p = 0.0004$ .

the percentage of sleep time with  $S_{a,O_2}$  below 90% ( $p = 0.005$ ). However, no significant correlations of these variables were found with either the other desaturation indices or the flow-volume indices. If the relationship between flow-volume variables and other data is considered, the only significant correlations were found in the OSA group between maximal nocturnal desaturation and the flow-volume indices: PIF ( $r = -0.48$ ;  $p = 0.004$ ); PEF % pred ( $r = -0.46$ ;  $p = 0.005$ ); and FIV1 % pred ( $r = -0.60$ ;  $p = 0.0004$ ) (figs. 1, 2 and 3). In this group also, a significant relationship ( $r = -0.54$ ;  $p = 0.002$ ) was found between the diameter of the soft palate (spd) with FIV1 % pred. In the group without OSA, there was no significant relationship between flow-volume indices and other variables.

### Discussion

To our knowledge, no published data are available on the relationship of the set of quantitative variables, obtainable from an inspiratory and expiratory flow-volume analysis and the spectre of indices from ENT, cephalometry and sleep  $O_2$  saturation measurements. The primary objective of our investigation was, therefore, the study of these inter-relationships and their interpretation. Our group of patients, selected for heavy snoring, was divided into a group with and a group without obstructive sleep apnoea (OSA). Although a selection criterion is arbitrary, habitual snoring may be considered as a preliminary stage toward transition to OSA. We did not use the apnoea-hypopnoea index as criterion for the presence of OSA for several reasons. Firstly, the amplitude of the flow reduction during a hypopnoea may depend on, *e.g.* body position and apparatus used. Secondly, the duration of an apnoea or hypopnoea interval is sometimes difficult to determine accurately. Therefore, we added a desaturation of more than 3% as criterion, which is easily and accurately measurable. The threshold for OSA, based on these two criteria, was set on five desaturations or more per hour. As further indices

for nocturnal desaturation, we used the maximal nocturnal desaturation and, in the OSA group, the percentage of sleep time with an  $S_{a,O_2} < 90\%$ .

The BMI ( $kg \cdot m^{-2}$ ) appeared to be significantly higher in the group with OSA compared to the group without. This finding is in accordance with previous studies [21]. Also, from investigations in heavy snorers, in which no distinction was made with respect to the presence of OSA, an enlarged BMI was considered as one of the prominent risk factors [21].

We found no significant differences between both groups for the cephalometric indices. Small differences or absence of difference between snorers with and without OSA were also found in other investigations [7, 8]. It was somewhat unexpected to find only one significant correlation between anatomical measurements and indices of pulmonary function (soft palate diameter *versus* FIV1). A general conclusion may, therefore, be that the cephalometric deviations are not reflected in the pulmonary function indices, whether reflecting upper airway resistance or not.

Although the collapsibility at the level of the tongue base (mtb) was just significantly higher in the OSA group than in the group without OSA, no significant relationships between the collapsibility variables and flow-volume indices were found. A possible explanation is given by the results of SHEPARD *et al.* [22], who studied, by computerized tomography imaging of the upper airways, the change in aperture at the level of the hard palate to the hypopharynx by applying either positive (+10  $cmH_2O$ ) or negative (-5  $cmH_2O$ ) transmural pressures. In a group of OSA patients and controls, they found no differences in change of the aperture under the influence of the changing transmural pressure, indicating no differences in the compliance of the airway at that level. Moreover, although the upper airway narrowing was carefully observed by fibroscopy, the ranking was certainly influenced by the subjective aspect and therefore primarily qualitative.

Oscillations on the flow-volume curves, which may be related to collapsibility of upper airway structures, were observed in our series with the same low frequency as described by KATZ *et al.* [11]. This confirms the low sensitivity for this phenomenon [1, 11]. Since it was observed in both groups, it seems to be related more to snoring than to OSA.

For the ventilatory response to  $CO_2$ , we confirmed in a subgroup of 11 patients the lack of correlation between OSA and the  $CO_2$  sensitivity ( $ScO_2$ ) during wakefulness [23]. Lowered  $ScO_2$  was previously found in OSA patients with hypercapnia [23, 24], but was not present in our patient group. It has to be stressed that, although chemical control mechanisms are generally assumed to play an important role during sleep [23, 25, 26], a relationship with the awake hypercapnic drive is still a matter of debate.

The significant correlation between baseline  $S_{a,O_2}$  and sleep time during which  $S_{a,O_2}$  was  $< 90\%$  can be explained by the pattern of the oxygen dissociation curve. Alveolar hypoventilation and, consequently, a decrease of arterial oxygen tension ( $Pa,O_2$ ) will cause an increased effect on  $S_{a,O_2}$  if this value is lower, and so nearer to the steeper part of this curve.

As mentioned above, like other authors [1, 11], we could not detect consistent significant correlations of flow-volume indices with either anatomical abnormalities or collapsibility indices. However, in the OSA group, we found significant correlations between the variables influenced by upper airway resistance (PEF in % pred, PIF and FIV<sub>1</sub> in % pred) and maximal desaturation during sleep. The maximal desaturation increased with a decrease in these variables (figs. 1–3). In the group without OSA, no significant correlations were seen. The borderline significant decrease in MEF<sub>50</sub> may be related to the smoking habits of both groups, causing an increase in peripheral airway resistance.

However, in both groups, we found a significant increase in the mean values for flow-volume variables influenced by upper airway resistance (PEF, FIV<sub>1</sub>). A possible explanation for this finding may be based on the study of SURATT *et al.* [27]. They measured the phasic genioglossal muscle group EMG in OSA patients and controls, and found, in the awake situation, markedly more phasic activity in the OSA group than in the controls. They concluded that, if the upper airway patency is precarious, a compensatory mechanism exists protecting the upper airways from a collapse. This compensatory mechanism means an increase of the tonic muscle activity, so that the forces acting to widen the oropharynx may be greater than in controls. This may explain the mean increase in the variables influenced by upper airway aperture.

A significant correlation with the effort-dependent flow-volume indices, mentioned above, has only been found for the maximal O<sub>2</sub> desaturation and not for the other desaturation indices. This relationship may be explained on the basis of a model of LONGOBARDO *et al.* [10], who simulated nocturnal periodic breathing depending on disturbances in chemical regulatory mechanisms and upper airway behaviour. In their model, the patency of the pharyngeal airway can be considered as a balance between the negative pharyngeal pressure, which promotes pharyngeal narrowing, and the genioglossal force, which acts to open the oropharynx [9, 10, 27]. In their view, the changes in chemosensitivity determining tonic activity of upper airway muscles, which take place especially during non-rapid eye movement (NREM) and rapid eye movement (REM) sleep, are crucial to the occurrence of OSA [9, 10, 27]. During wakefulness, the tonic activity of the upper airway muscles is sufficiently high. The response of these muscles to chemical stimuli will then be relatively unimportant.

In patients with OSA, both craniomandibular abnormalities of skeletal and soft tissue morphology [1–8] and impaired chemosensitivity, causing lowered nocturnal tonic activity of upper airway muscles, may be present. The resulting increase in upper airway collapsibility then leads to narrowing and eventually closure during sleep due to the negative transmural pressure during inspiration. Arousal effects and increase in arterial carbon dioxide tension (Pa<sub>a</sub>CO<sub>2</sub>) and decrease in Pa<sub>a</sub>O<sub>2</sub> as chemical stimuli will cause a reopening after the apnoea or hypopnoea period. Narrowing and closure will be facilitated if the baseline upper airway aperture is small. Because

the effort-dependent flow-volume indices are sensitive indicators of upper airway resistance, a decrease in these indices most probably reflects a decrease in baseline upper airway aperture. It has to be realized, as explained above, that in OSA patients this decrease is superimposed on a widening effect by compensating mechanisms which are purportedly present. A decrease in upper airway aperture generates a more negative transmural pressure over the upper airways during inspiration, which promotes their narrowing and eventual closure.

Most probably, not only the onset of apnoea or hypopnoea is facilitated but a stronger stimulus will also be needed to restore normal ventilation. This may lead to a lengthening of the apnoea or hypopnoea period, thereby causing a larger dip in the Sa<sub>a</sub>O<sub>2</sub>. We did not find a significant correlation between baseline Sa<sub>a</sub>O<sub>2</sub> and either maximal desaturation or flow-volume indices. Based on the pattern of the O<sub>2</sub> dissociation curve, an increased maximal desaturation should be expected in the case of a lower baseline Sa<sub>a</sub>O<sub>2</sub>. It is likely that the baseline Sa<sub>a</sub>O<sub>2</sub> is related more to the overall nocturnal desaturation (we found a positive correlation with sleep time with Sa<sub>a</sub>O<sub>2</sub> <90%) and only increases the variance in the relationship between maximal nocturnal desaturation and flow-volume indices.

Although we realize that the explanation is speculative, extending the model by incorporating the area of the oropharyngeal aperture in the model of LONGOBARDO *et al.* [10] may improve its usefulness and, perhaps, strengthen our hypothesis. As LONGOBARDO *et al.* [10] show in their model, the periodicity of the apnoeas is more likely to be related to the chemical regulatory mechanisms.

In conclusion, this study has again confirmed the lack of diagnostic value of the flow-volume indices in patients with OSA. However, the behaviour of the variables influenced by upper airway resistance in relation to maximal O<sub>2</sub> desaturation may be explained in terms of the mechanisms which determine the obstructive sleep apnoea syndrome.

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