

Respiratory impedance response to continuous negative airway pressure in awake controls and OSAS

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Respiratory impedance response to continuous negative airway pressure in awake controls and OSAS. A.M. Lorino, F. Lofaso, E. Dahan, A. Harf, H. Lorino. ©ERS Journals Ltd 2001.

ABSTRACT: The aim of the study was to determine whether the response of respiratory impedance (Z_{rs}) to decreasing levels of continuous negative airway pressure (CNAP) during wakefulness, differs in controls and subjects with obstructive sleep apnoea syndrome (OSAS).

Z_{rs} was measured by the forced oscillation technique (4–32 Hz) in 15 controls and 21 patients with OSAS (apnoea/hypopnoea index >20 per sleep hour) with normal lung function, in the basal state and with application of decreasing CNAP of -5, -10, and -15 hPa. Respiratory resistance was extrapolated to 0 Hz (R_0) and estimated at 16 Hz (R_{16}) by linear regression analysis of respiratory resistive impedance versus frequency. Respiratory elastance (E_{rs}) and inertance (I_{rs}) were estimated by multilinear regression analysis of respiratory reactance versus frequency, and resonance frequency (RF) was determined as $RF = (1/2\pi)(E_{rs}/I_{rs})^{0.5}$.

In both groups, R_0 , R_{16} , E_{rs} and RF significantly increased as the CNAP level decreased ($p < 0.0001$ for all). R_0 , E_{rs} , and RF increased significantly more in OSAS than in controls ($p < 0.01$, 0.001 , and 0.0001 , respectively), independently of the severity of obesity. Receiver operator characteristic curves showed that the parameter which best detected OSAS was RF, with a sensitivity of 81% and 93% specificity for the 13.6 Hz cut-off point.

The results of the present study suggest that the response of respiratory impedance to decreasing continuous negative airway pressure levels, might allow detection of obstructive sleep apnoea syndrome in subjects with normal lung function.

Eur Respir J 2001; 17: 71–78.

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Keywords: Continuous negative airway pressure
forced oscillations
obstructive sleep apnoea syndrome
respiratory elastance
respiratory resistive impedance

Received: March 14 2000

Accepted after revision September 16 2000

Obstructive sleep apnoea/hypopnoea syndrome (OSAS) is characterized by the occurrence of repetitive upper airway (UA) narrowing and/or closure during sleep. Obstructive respiratory events are generally explained by the inefficiency of the dilating muscles in counterbalancing the tendency of the pharyngeal airway to collapse, due to the inspiratory decrease in UA transmural pressure [1]. The main factors predisposing subjects to OSAS appear to be: 1) a reduction of UA calibre [2]; 2) an increase in UA resistance, as well as in pulmonary and respiratory resistances [3–5]; 3) an increase in UA compliance [4, 6, 7]; and 4) dysfunction of the UA dilating muscles [8].

The application of continuous negative airway pressure (CNAP) at the airway opening generates a subatmospheric intraluminal UA pressure that simulates the conditions promoting the occurrence of obstructive respiratory events. The effect of CNAP on pharyngeal cross-sectional area and resistance have been widely investigated in control and OSAS subjects [4, 8–11], but, to the authors' knowledge, CNAP-induced changes in the respiratory mechanical parameters remain poorly documented [12]. The aim of the present study was, therefore, to investigate whether the

response of respiratory mechanics to decreasing CNAP levels differs between control and OSAS subjects, and might provide a predictive index of OSAS. To this end, the forced oscillation technique (FOT) was used, which allows easy measurement of respiratory impedance (Z_{rs}) during CNAP application.

Materials and methods

Subjects

The authors studied 36 subjects in two groups. The control group consisted of 15 asymptomatic healthy subjects (9 males), aged 31–57 yrs (mean \pm SD 47 ± 12 yrs), with a body mass index (BMI) < 29 kg·m⁻², (mean 24.1 ± 2.9 kg·m⁻²), and no upper or lower respiratory complaints. None of the subjects were habitual snorers, and none complained of the diurnal or nocturnal symptoms seen with sleep apnoea syndrome. The OSAS group consisted of 21 patients with moderate-to-severe OSAS (17 males) aged 34–78 yrs (mean 54.6 ± 10.9 yrs). This group was initially divided into two subgroups according to the subjects' BMI. OSAS₁

($n=11$) comprised patients with $BMI < 29 \text{ kg}\cdot\text{m}^{-2}$ (mean $25.0 \pm 2.3 \text{ kg}\cdot\text{m}^{-2}$), and $OSAS_2$ ($n=10$), those with $BMI \geq 29 \text{ kg}\cdot\text{m}^{-2}$ (mean $32.7 \pm 3.9 \text{ kg}\cdot\text{m}^{-2}$). All patients had normal lung volumes and forced expiratory flow rates ($\geq 80\%$ of predicted values), and no history of cardiopulmonary disease. Their apnoea/hypopnoea index, established previously on the basis of overnight polysomnography, ranged from 20–87 per sleep hour (mean 44 ± 25 per sleep hour). The experimental protocol had the prior approval of the authors' hospital Ethics Committee, and all subjects gave informed consent.

Respiratory resistance measurement

Z_{rs} was measured at the mouth by FOT. The pseudo-random forced flow used in this study was composed of 29 harmonics (4–32 Hz), with enhanced amplitudes at the lower frequencies, to limit the influence of spontaneous breathing. The forced signal, generated by a digital-to-analogue converter, excited, through a power amplifier, a 50-W loudspeaker (Audax HM 130 XO, Château du Loir, France) enclosed in a 25-litre rigid chamber and placed in parallel with the CNAP device, as previously described [13]. Mouth flow was measured with a screen pneumotachograph (resistance $= 0.35 \text{ hPa}\cdot\text{L}^{-1}\cdot\text{s}$; Jaeger, Wurzburg, Germany) connected to a differential pressure transducer ($\pm 70 \text{ hPa}$; Sensym SCX 01D, Sunnyvale, CA, USA), and mouth pressure by a similar pressure transducer referenced to the atmosphere. The pneumotachograph and the tubing were flushed by a constant bias flow ($0.5 \text{ L}\cdot\text{s}^{-1}$). Pressure and flow data were collected over 16 s periods and high-pass filtered (3rd order, cut-off frequency 3.5 Hz) to eliminate the breathing noise. A fast Fourier transform algorithm was applied to adjacent 4 s periods. Impedance data were calculated from the auto- and cross-spectra of pressure and flow, averaged over 3–4 manoeuvres, and retained for analysis when coherence was ≥ 0.9 [14]. Respiratory resistance (R_{rs}) was submitted to linear regression analysis *versus* frequency over the 4–16 and 17–32 Hz frequency ranges. R_{rs} extrapolated to 0 Hz (R_0) was derived from the first linear regression analysis, and R_{rs} estimated at 16 Hz (R_{16}), from the second one [15]. The frequency dependence of R_{rs} was assessed by the difference $\Delta R_{rs} = R_0 - R_{16}$. Respiratory elastance (E_{rs}) and inertance (I_{rs}) were estimated by multilinear regression analysis of respiratory reactance *versus* frequency. Resonance frequency (RF) was determined as the frequency corresponding to the zero value of respiratory reactance, *i.e.* as $RF = (1/2\pi)(E_{rs}/I_{rs})^{0.5}$.

Experimental protocol

Each subject was studied in the sitting position under four successive conditions: in the basal state (CNAP₀), and with decreasing levels of CNAP of -5, -10, and -15 hPa (CNAP₋₅, CNAP₋₁₀, and CNAP₋₁₅, respectively) applied at the mouth. CNAP was generated by an adjustable vacuum source, set at the negative pressure required before the subject was connected to the breathing circuit, and continuously monitored with a manometer. The subject, wearing a nose clip and firmly

supporting his cheeks with his hands, was then connected to the CNAP device, and asked to breathe quietly and not to fight the applied pressure. After a 30 s period of adaptation to CNAP, forced oscillation was applied for 16 s, and the subject was disconnected from the CNAP device for 2 min. This sequence was repeated 3–4 times at each CNAP level, and a 5 min period was allowed to pass after the last release from one CNAP level before the first application of the next CNAP level.

Data analysis

Values are mean \pm SEM, except when otherwise indicated. Statistical analysis of data was performed using linear regression analysis, analysis of variance, paired t-tests, and unpaired t-tests. A value of $p < 0.05$ was considered significant.

The sensitivity and specificity of possible cut-off points for R_0 , E_{rs} , and RF, to discriminate between control subjects and OSAS patients, were studied using the receiver operator characteristic (ROC) curve [16]. The ROC curve allowed the visualization of the true positive rate (sensitivity) as a function of the false positive rate (1-specificity) for the different values of the respiratory parameters, and the determination of the cut-off point corresponding to the best compromise between sensitivity and specificity, defined as the closest point of the curve to the upper left hand corner.

Results

There was no significant difference in age between controls and patients with OSAS. No significant difference was observed either for BMI between controls and OSAS₁, but BMI was significantly higher in OSAS₂ than in controls and OSAS₁ ($p < 0.0001$ for both).

With CNAP₀, R_0 and R_{16} were significantly higher in groups OSAS₁ and OSAS₂ than in controls, but the small difference between OSAS₁ and OSAS₂ was not significant (fig. 1). Within each group, no significant difference was observed between R_0 and R_{16} . E_{rs} and RF were slightly but significantly higher in group OSAS₂ than in controls and OSAS₁ (fig. 2), and I_{rs} was slightly but significantly lower in OSAS₂ than in controls (0.012 ± 0.001 *versus* $0.014 \pm 0.001 \text{ hPa}\cdot\text{s}^2\cdot\text{L}^{-1}$).

A typical response of respiratory impedance to decreasing CNAP levels, obtained in a representative OSAS subject, is shown in figure 3. Interestingly, the differences observed for the respiratory mechanical parameters at CNAP₀ between OSAS₁ and OSAS₂, disappeared as the CNAP level decreased, and no significant differences were observed for the mechanical parameter responses to decreasing CNAP levels between OSAS₁ and OSAS₂ (figs. 1 and 2). Therefore, in what follows, the results will be presented for controls and OSAS, without making a distinction between OSAS₁ and OSAS₂.

In both control and patient groups, R_0 , R_{16} , and the difference $\Delta R_{rs} = R_0 - R_{16}$ increased significantly as the CNAP level decreased ($p < 0.0001$ for all, fig. 4). The CNAP-induced increases in R_0 and ΔR_{rs} were significantly greater in patients than in controls ($p < 0.01$

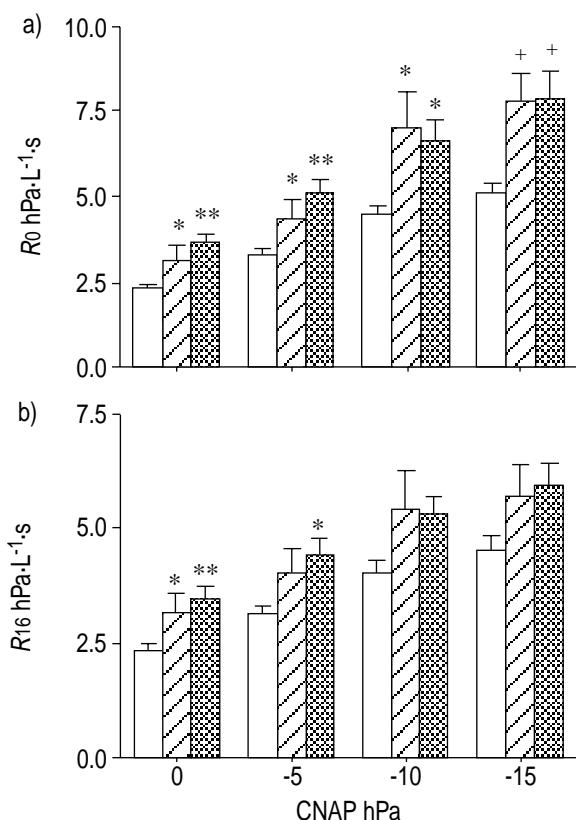


Fig. 1. – Respiratory resistive impedance a) extrapolated to 0 Hz (R_0) and b) estimated at 16 Hz (R_{16}), in the basal state (continuous negative airway pressure (CNAP)=0) and with CNAP levels of -5, -10, and -15 hPa. Obstructive sleep apnoea syndrome (OSAS)₁ patients (▨) with body mass index (BMI) <29 kg·m⁻²; OSAS₂ patients (▩) with BMI ≥29 kg·m⁻²; controls (□). Data are presented as mean±SEM. *: p<0.05 versus controls; **: p<0.01 versus controls; +: p<0.005 versus controls.

and 0.001, respectively). E_{rs} and RF significantly increased as the CNAP level decreased (p<0.0001 for both) (fig. 5), whereas no significant change was observed for I_{rs} . The CNAP-induced increases in E_{rs} and RF were significantly greater in patients than in controls (p<0.001 and 0.0001, respectively).

At each CNAP level, a highly significant linear relationship was found in all 36 subjects, between E_{rs} and R_0 on the one hand, and RF and R_0 on the other, (p<0.0001 for both), and the corresponding correlation coefficients increased as the CNAP level decreased, from $r^2=0.48$ and 0.39 at CNAP₀, respectively, to $r^2=0.81$ and 0.80 at CNAP₋₁₅ (fig. 6).

ROC curves for R_0 , E_{rs} , and RF at CNAP₋₁₅ show how these parameters could discriminate between OSAS patients and control subjects (fig. 7). OSAS patients were detected optimally by the cut-off points of 6.6 hPa·L⁻¹·s for R_0 with a 67% sensitivity and a 93% specificity, 66.7 hPa·L⁻¹ for E_{rs} with a 90% sensitivity and a 67% specificity, and 13.6 Hz for RF with an 81% sensitivity and a 93% specificity.

Discussion

To the authors' knowledge, this is the first study which compares the responses of respiratory impedance to decreasing CNAP levels in OSAS patients and

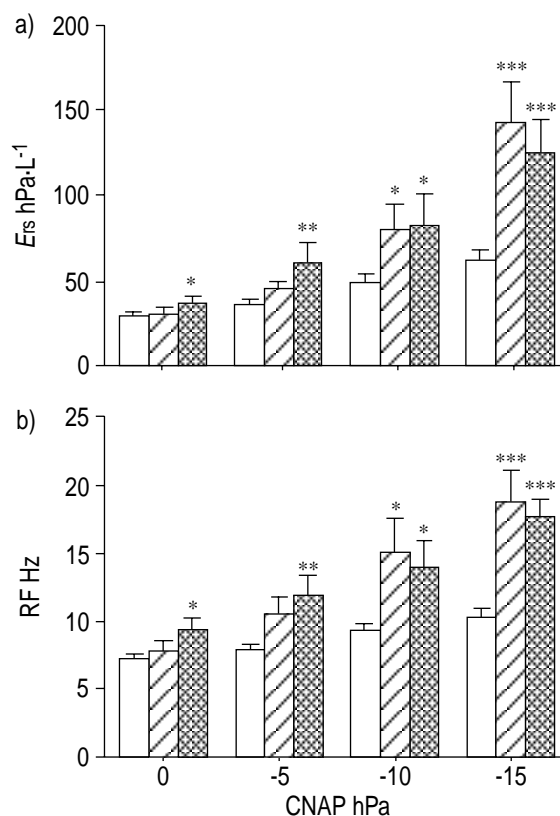


Fig. 2. – a) Respiratory elastance (E_{rs}) and b) resonance frequency (RF) in the basal state (continuous negative airway pressure (CNAP)=0) and with CNAP levels of -5, -10, and -15 hPa. Obstructive sleep apnoea syndrome (OSAS)₁ patients (▨) with body mass index (BMI) <29 kg·m⁻²; OSAS₂ patients (▩) with BMI ≥29 kg·m⁻²; controls (□). Data are presented as mean±SEM. *: p<0.05 versus controls; **: p<0.01 versus controls; ***: p<0.001 versus controls.

normal subjects, and which demonstrates that resonance frequency best allows discrimination between the two groups. The ages of controls and OSAS patients did not differ but the male:female ratio was lower in the controls than in the patients. However, it may be assumed that this difference did not influence the authors' results, since a previous study has shown that, despite the anatomical and functional differences of the UA in males and females, the R_{rs} responses to decreasing CNAP levels were similar in both sexes [12].

Initially, the authors divided the patients into two groups, in order to dissociate the respective influences of OSAS and BMI on the mechanical respiratory parameter values. That way, any difference between controls and OSAS₁ could be attributed to the presence of OSAS, whereas any difference between OSAS₁ and OSAS₂ could be attributed to the severity of obesity.

It would have been more relevant to the clinical situation of OSAS if impedance measurements had been made in the supine position and *via* the nose. However, both the supine position and application of CNAP tend to promote nasal congestion, which would have resulted in unstable R_{rs} values. Furthermore, it may be assumed that the influence of nasal congestion on R_{rs} would have depended on the CNAP level and thereby biased the authors' results. In addition, neck position is more difficult to control when supine, and

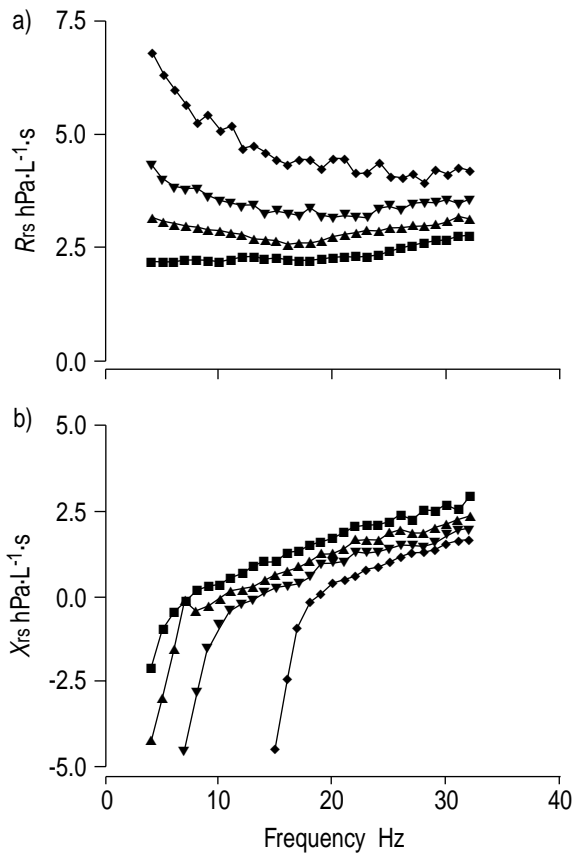


Fig. 3. – Typical frequency responses of a) respiratory resistive impedance (R_{rs}) and b) reactance (X_{rs}) to decreasing continuous negative airway pressure (CNAP) levels of 0, -5, -10 and -15 hPa, in a representative obstructive sleep apnoea syndrome subject. ■: CNAP 0 hPa; ▲: CNAP -5 hPa; ▼: CNAP -10 hPa; ◆: CNAP -15 hPa.

neck extension or flexion is known to affect UA geometry [17], and consequently R_{rs} . Lastly, compared to the sitting position, the supine position induces an immediate decrease in end-expiratory lung volume (EELV), and consequently increases in R_{rs} , E_{rs} , I_{rs} , and RF [18], which might have affected the responses of these parameters to decreasing CNAP levels.

The FOT was used, as opposed to the classical oesophageal balloon technique for assuming respiratory mechanics, because: 1) FOT is a noninvasive method, *i.e.* it does not necessitate the placement of a nasopharyngeal catheter which may influence UA resistance during CNAP application [19]; 2) FOT provides respiratory parameters, *i.e.* parameters which describe the mechanical behaviour of both the pulmonary component and the chest wall component, including respiratory muscles; and 3) with appropriate frequencies, FOT allows measurement of Newtonian respiratory resistance, and delayed respiratory resistance not including tissue viscoelasticity [15, 20], as well as respiratory reactance and its derived parameters. The authors, therefore, chose pseudorandom forced flow rather than a monosinusoidal oscillation, in order to study the frequency dependence of respiratory resistance, and to determine the parameters characterizing respiratory reactance, namely respiratory elastance,

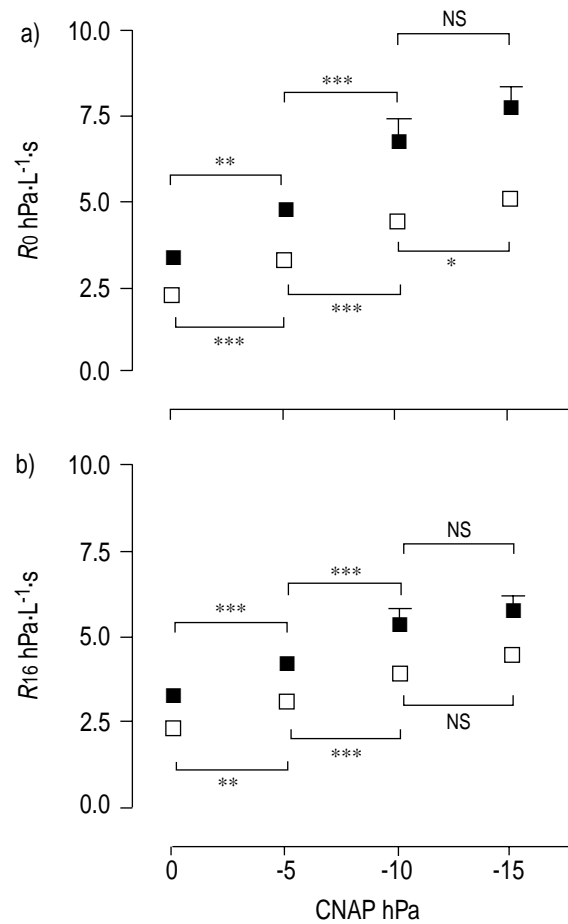


Fig. 4. – Respiratory resistive impedance a) extrapolated to 0 Hz (R_0), and b) estimated at 16 Hz (R_{16}), in the basal state (continuous negative airway pressure (CNAP)=0), and with CNAP levels of -5, -10 and -15 hPa, in obstructive sleep apnoea patients (■) and controls (□). Data are presented as mean \pm SEM. *: $p < 0.05$; **: $p < 0.01$; ***: $p < 0.001$; NS: nonsignificant difference.

inertance, and resonance frequency. However, the pseudorandom forced flow did not allow partitioning of airway resistance into inspiratory and expiratory resistances.

The authors chose two complementary indices of respiratory resistance, namely R_0 and R_{16} . Indeed, R_{rs} , which was roughly constant over 4–32 Hz in subjects with normal lungs, showed negative frequency dependence when gas redistribution within the airways occurred, as a result of series or parallel inhomogeneities [21]. As this frequency dependence occurs mainly below 16 Hz, R_{16} can be considered to reflect Newtonian respiratory resistance, and R_0 , total respiratory resistance, *i.e.* Newtonian resistance plus the delayed airflow resistance resulting from gas redistribution, when present [15, 20]. It also appeared interesting to consider the parameters derived from respiratory reactance. Indeed, parallel variations of R_0 and RF have been reported in the course of bronchial challenge tests to inhaled methacholine [22], and any increase in tissue elastance is associated with an increase in E_{rs} , and thereby in RF.

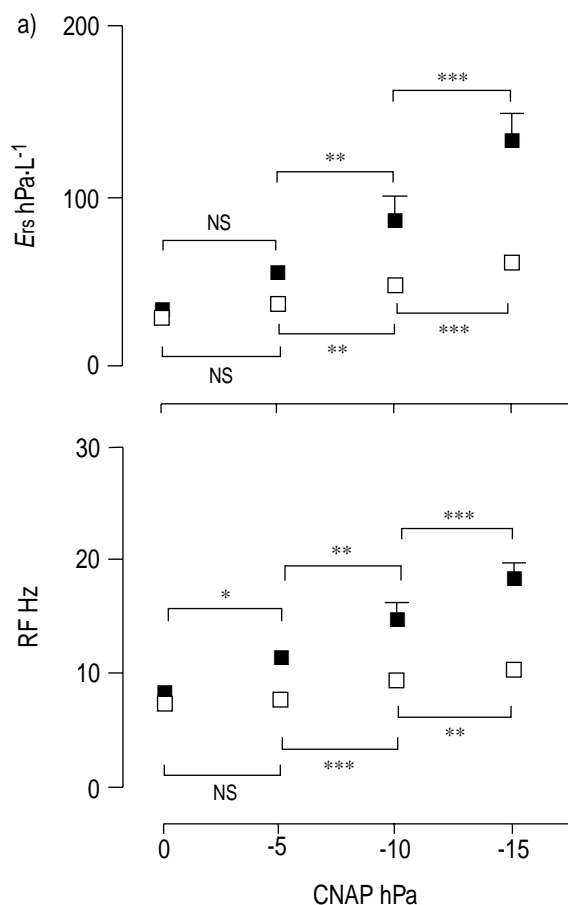


Fig. 5. – a) Respiratory elastance (E_{rs}) and b) resonance frequency (RF), in the basal state (continuous negative airway pressure (CNAP)=0) and with CNAP levels of -5, -10, and -15 hPa, in obstructive sleep apnoea syndrome patients (■) and controls (□). Data are presented as mean \pm SEM. *: $p < 0.05$; **: $p < 0.01$; ***: $p < 0.001$; NS: nonsignificant difference.

Basal respiratory impedance

The basal R_0 , E_{rs} , and I_{rs} values are in the range of those previously reported in normal subjects with or without minimal obesity [18, 23]. The fact that basal R_0 , and R_{16} values were significantly higher in OSAS₁ and OSAS₂ groups than in controls, may be attributed to the OSAS factor. This result is in accordance with previous reports that for a comparable BMI, OSAS subjects have smaller pharyngeal cross-sectional areas [2] and higher R_{rs} values than non-OSAS subjects [5]. The fact that both basal R_0 and R_{16} were not significantly different in OSAS₁ and OSAS₂ groups must be interpreted with caution, due to the small numbers in the groups. However, it suggests that airway geometry might be less influenced by the obesity factor than by the OSAS factor in subjects with normal lung volumes during wakefulness.

No significant difference was observed between basal R_0 and R_{16} values in controls, OSAS₁, and OSAS₂, which illustrates the fact that R_{rs} was not frequency dependent. This result reflects homogeneous distribution of gas flow within the respiratory system [21], and

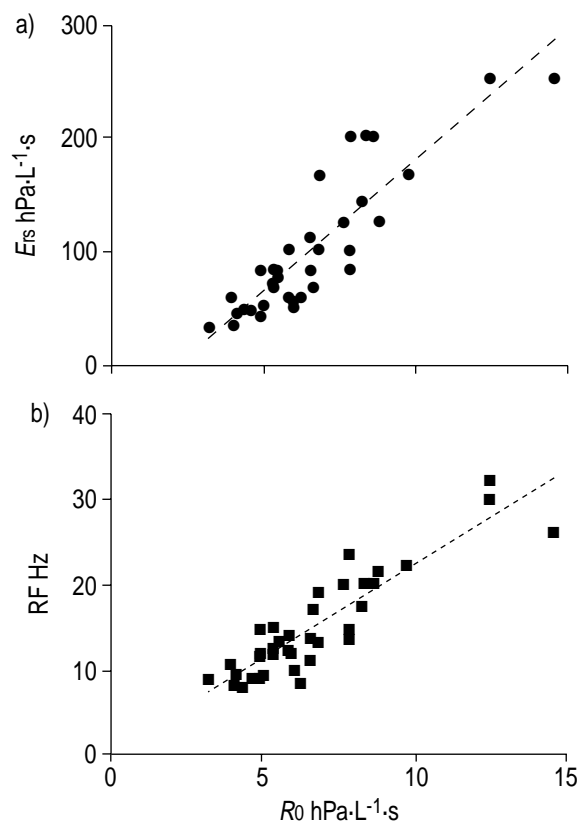


Fig. 6. – a) Respiratory elastance (E_{rs}) and b) resonance frequency (RF) at the continuous negative airway pressure level of -15 hPa (CNAP) plotted in relation to respiratory resistive impedance extrapolated to 0 Hz (R_0) at CNAP₋₁₅. Points represent data from individual subjects, and the straight lines are regression lines. a) $E_{rs} = 23.2R_0 - 51.3$, $r^2 = 0.81$, $p < 0.0001$; b) $RF = 2.18R_0 + 0.43$, $r^2 = 0.80$, $p < 0.0001$.

would be expected in subjects with no detectable airway obstruction.

Only the mechanical parameters derived from respiratory reactance, namely E_{rs} , I_{rs} , and RF, which were significantly different in OSAS₁ and OSAS₂, were influenced by obesity (fig. 2). These results are in accordance with those previously reported by ZERAH *et al.* [23] who attributed obesity-related increases in E_{rs} mainly to those in chest wall elastance.

Respiratory response to decreasing continuous negative airway pressure levels

The CNAP-induced increases in R_0 and R_{16} presently observed in controls (figs. 1 and 4) are comparable to those previously reported in a similar study [12], in which it was demonstrated that a direct lung volume effect on airway resistance could not totally explain the increase in R_{rs} [12], and that other factors were probably involved. These may include: 1) a narrowing of extrathoracic airways directly resulting from the CNAP-induced decrease in UA transmural pressure, since, for a given transrespiratory pressure, supralaryngeal resistance increases more during CNAP than during continuous positive extrathoracic pressure [9]; and 2) an indirect effect of lung deflation, *i.e.* an

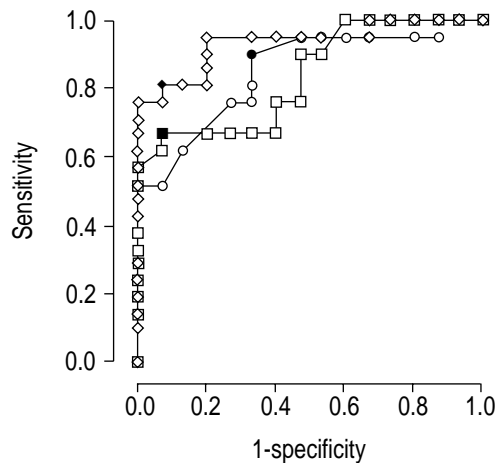


Fig. 7. – Receiver operator characteristic (ROC) curves for the respiratory parameters at the continuous negative airway pressure (CNAP) levels of -15 hPa to discriminate between obstructive sleep apnoea syndrome (OSAS) patients and normal subjects. \square : respiratory resistive impedance extrapolated to 0 Hz (R_0); \circ : respiratory elastance; and \diamond : resonance frequency. The closed symbols represent optimal cut-off points.

additional increase in oropharyngeal resistance possibly due to an increase in UA collapsibility involving mechanical linkages between the thorax and the UA [24]. However, it is likely that the R_{rs} response to CNAP also resulted partly from an increase in tissue resistance (R_{ti}) due to the CNAP-induced decrease in lung volume [25].

The CNAP-induced increases in E_{rs} reflect a decrease in respiratory compliance, *i.e.* in gas, and/or lung, and/or chest wall compliance. Indeed, CNAP application induces significant decreases in EELV [12], and consequently in gas compliance. Furthermore, these decreases in EELV have already been reported to result in reduced lung compliance under CNAP, due to the sigmoid shape of the lung volume/transpulmonary pressure relationship [26]. Besides, decreases in respiratory reactance have previously been observed during resistive or elastic loading, and attributed to an increase in tissue elastance resulting from increased respiratory muscle activity [27]. As it has been reported that CNAP application results in an increase in diaphragmatic and parasternal intercostal electromyographic activity [10, 28], the E_{rs} response to CNAP presently observed may be explained by the enhanced activity of inspiratory muscles. As I_{rs} remained unchanged when the CNAP level was decreased, the significant increases observed in RF directly result from those in E_{rs} .

The fact that ΔR_{rs} increased significantly as the CNAP level decreased, *i.e.* that R_{rs} became more and more frequency dependent, may be attributed to: 1) the increase in R_{ti} resulting from reduced lung volume, which has been reported to be more pronounced at the lower frequencies [25]; and 2) the occurrence and development of series and/or parallel gas redistribution [21]. Series gas redistribution is mainly due to UA shunt compliance, whose influence on R_{rs} was probably reduced under CNAP, due to the increased activity of UA dilating muscles [10]. Consequently, it is more

probable that parallel gas redistribution developed within intrathoracic airways, as a result of the pulmonary inhomogeneities promoted by the CNAP-induced decrease in lung volume.

An interesting result is that none of the responses of the respiratory mechanical parameters to decreasing CNAP levels were significantly different in groups OSAS₁ and OSAS₂. This suggests that, whereas in the basal state, E_{rs} , I_{rs} , and RF were slightly influenced by the obesity level in subjects with normal lung volumes, at low CNAP levels they depend mainly on the physiological conditions of the ventilation, namely decreased lung volume and increased respiratory muscle activity. Consequently, any difference between the respiratory responses to CNAPs in control and OSAS subjects can be considered independent of the obesity level.

The improvement in the quality of the linear relationship between E_{rs} and R_0 when decreasing the CNAP level may be explained as follows: R_0 represents the resistance to be overcome by the respiratory muscles, to the exclusion of the delayed resistance due to the tissue viscoelastic properties [15]; E_{rs} partly reflects respiratory muscle activity; both R_0 and E_{rs} increase as the CNAP level is lowered. As I_{rs} remained unchanged, the improvement in the quality of the linear relationship between RF and R_0 when decreasing the CNAP level may be similarly explained.

Comparisons between control and obstructive sleep apnoea syndrome subjects

Surprisingly, no significant difference was observed between the two groups regarding the response of R_{16} to decreasing CNAP levels. An enhanced response of UA resistance to negative transmural pressures might be expected in OSAS patients whose UAs are narrower and more collapsible [4, 8]. Therefore, it could be speculated that UA patency was maintained at the cost of a greater increase in UA muscle electromyographic activity in OSAS than in normal subjects, as previously observed in patients during sleep [29]. The CNAP-induced increase in UA muscle activity appears to result from the simultaneous occurrences of the decrease in lung volume, the low intraluminal pressure, and the increase in diaphragmatic activity, since it has been reported that: 1) the active reduction of EELV results in increased UA muscle activity [30]; 2) when the CNAP-induced decrease in EELV is prevented by applying identical pressure to the body surface, UA muscle activity is enhanced, despite the absence of change in diaphragmatic activity [11]; and 3) UA muscle activity responds to CNAP in a manner similar to diaphragmatic activity [10]. The difference between the increases in E_{rs} observed in the two groups strongly suggests that the CNAP-induced increase in diaphragmatic activity was greater in OSAS than in control subjects. In this connection, it has been reported that the activation of UA dilators is reflected by indices that quantify the central inspiratory drive, and that for the same increase in the central inspiratory drive, the decrease in pharyngeal resistance is more marked in OSAS patients than in normal subjects [31]. It is worth

noting that, during inspiration, the compensatory increase in activity of the airway dilator muscles minimizes the suction effect of CNAP on extrathoracic airways. Consequently, the CNAP-induced increase in UA resistance was probably less than during expiration. The resistance values were, however, determined over the entire ventilatory cycle, and did not allow partitioning of airway resistance into inspiratory and expiratory resistances. Although no significant difference was observed between OSAS patients and control subjects regarding the responses of R_{16} to decreasing CNAP levels, may it be speculated that the respective contributions of inspiratory and expiratory resistances to R_{16} might have been different in OSAS and normal subjects.

The fact that the CNAP-induced increases in R_0 and ΔR_{rs} were significantly greater in OSAS than in controls, might be due to a greater increase in R_{ti} and/or delayed airflow resistance resulting from intrapulmonary gas redistribution at low lung volume. OSAS may be an independent risk factor for small airway disease as assessed by abnormally low expiratory flow rates at 50 and 25% of the vital capacity [5]. Subclinical abnormalities of distal airways might thus be revealed with application of CNAP in OSAS subjects with normal lung function. Besides, the fact that the decreases in EELV were more marked in the patients than in the controls, cannot be excluded.

When comparing patients to controls, the CNAP-induced increases in E_{rs} and RF were significantly more marked than those in R_0 , probably because R_0 does not take into account the resistive component due to the tissue viscoelastic properties [15]. This component, which varies with lung volume [32], is partly responsible for the respiratory effort that E_{rs} , and consequently RF, may be assumed to reflect.

When comparing the ROC curves for R_0 , E_{rs} , and RF at CNAP₁₅, to discriminate between control and OSAS patients (fig. 7), it may be observed that the best results were obtained for RF which, for a given specificity, identified OSAS patients with the highest sensitivity. This shows that although highly correlated (fig. 6), the different indices derived from respiratory resistance and reactance do not provide redundant information.

In conclusion, this study demonstrated that the responses of respiratory impedance to decreasing continuous negative airway pressure levels differ in obstructive sleep apnoea syndrome and control subjects during wakefulness, and that this difference cannot be attributed to the obesity level. The results suggest that the response of respiratory impedance to decreasing continuous negative airway pressure, and more particularly the response of resonance frequency, which probably reflects the increase in respiratory muscle activity, might allow discrimination between control and obstructive sleep apnoea syndrome subjects with normal lung function. Thus, the application of subatmospheric pressures might be useful as a screening test for obstructive sleep apnoea syndrome during wakefulness, although additional studies including a larger number of subjects are needed before it can be recommended for this purpose.

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