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Noninvasive assessment of respiratory resistance in severe chronic respiratory patients with nasal CPAP

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Noninvasive assessment of respiratory resistance in severe chronic respiratory patients with nasal CPAP. R. Farré, E. Gavela, M. Rotger, M. Ferrer, J. Roca, D. Navajas. ©ERS Journals Ltd 2000.

ABSTRACT: Noninvasive measurement of respiratory resistance during nasal ventilatory support could be useful to assess the mechanical status of the patient and to optimize the ventilator settings. The aim was to investigate whether the forced oscillation technique (FOT) applied through a nasal mask allows reliable noninvasive estimation of respiratory resistance (*R*rs) in patients with severe chronic respiratory disease.

FOT *R*rs (5 Hz) and lung resistance (*R*L) measured simultaneously from spontaneous breathing signals by an oesophageal balloon were compared in eight patients with chronic obstructive pulmonary disease and in six patients with a restrictive ventilatory defect due to chest wall disease. Measurements were performed in sitting and supine postures during application of nasal continuous positive airway pressure (CPAP): 4, 8 and 12 cmH$_2$O in obstructive patients and 4 cmH$_2$O in restrictive patients.

In the restrictive patients *R*rs and *R*L (in cmH$_2$O·s·L^{-1}) were virtually coincident: mean±SD, 12.6±6.1 and 11.6±6.6 (r=0.96) in sitting and 9.7±3.1 and 10.2±3.3 (r=0.92) in supine posture, respectively. In the obstructive patients (CPAP = 4 cmH$_2$O), *R*rs slightly underestimated *R*L: mean±SD, 11.5±5.9 and 14.4±16.8 (r=0.92) in sitting and 15.0±9.8 and 21.1±12.6 (r=0.96) in supine posture, respectively. Similar results were found at CPAP = 8 and 12 cmH$_2$O.

The results obtained in patients with resistance values in the range typically found in nasal ventilatory support suggest that forced oscillation technique could be valuable to noninvasively estimate a patient's respiratory mechanical resistance.
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Nasal positive pressure ventilation is increasingly being used in the noninvasive management of patients with acute or chronic respiratory failure [1, 2]. As the ventilator is an artificial pump to support the muscle activity of the spontaneous breathing patient, adapting the ventilator output to the mechanical status of the patient would facilitate ventilator-patient matching. To this end, the measurement of total respiratory resistance and reactance of the patient would help to improve the settings of the ventilator. The interest of noninvasively assessing respiratory mechanics to optimize the efficiency of ventilatory support is enhanced in ventilation strategies, such as proportional assist ventilation [3], in which the pressure generated by the ventilator is adapted to the resistive and elastic properties of the patient's respiratory system. Unfortunately, the most conventional techniques available do not allow the noninvasive assessment of resistance in nonparalysed patients [4]. Indeed, the conventional method for exploring respiratory mechanics by means of an oesophageal balloon is not convenient in the context of noninvasive mechanical ventilation. Moreover, simpler procedures not requiring an oesophageal balloon such as body plethysmography or the interrupter technique are not applicable in spontaneously breathing patients under ventilatory support. Consequently, in the absence of a simple method for noninvasively assessing respiratory mechanics, the ventilator settings cannot be tailored to the mechanical conditions of the patient.

The forced oscillation technique (FOT) [5, 6] is the only method available at present for noninvasively assessing the mechanical properties of the respiratory system in nonparalysed patients subjected to ventilatory support through a nasal mask. As it is easily applicable and provides automatic on-line estimation of respiratory resistance, FOT is a potentially useful tool for evaluating the mechanical status of the patient during nasal noninvasive mechanical ventilation. Nevertheless, the FOT data currently available do not provide evidence of the reliability of the technique in this particular application since in most studies FOT was applied through a mouthpiece instead of a nasal mask. This point concerning the ventilator-patient interface is of crucial importance. Indeed, it has been shown that when FOT is applied through a mouthpiece in patients with increased resistance this technique results in a considerable underestimation of the value of the patient's resistance [7] due to the shunt induced by the extrathoracic upper airways [8, 9]. By contrast, very recent studies where FOT was applied through a nasal mask in patients with obstructive sleep apnoea have shown that this technique provided a useful index to quantify the changes of upper airway obstruction [10–12]. These data suggest that the artefactual role played by the extrathoracic upper airways in FOT measurements is reduced when breathing through a nasal mask owing to the by-pass of the wall-compliant oral cavity. However, recent data in sleep apnoea patients indicated that total resistance measured by FOT at 16 Hz underestimated lung resistance (R_L) measured by the oesophageal balloon, although both resistance indices showed a considerable correlation [12]. This discrepancy between both resistance estimates could be partially due to the relatively high forced oscillation frequency used and partially due to the fact that the measurements were made under the typical flow limitation conditions found during inspiration in patients with obstructive sleep apnoea. The aim of this work was to investigate whether FOT applied through a nasal mask at the relatively low frequency of 5 Hz allows reliable noninvasive estimation of respiratory resistance in patients with increased impedance, potentially tributary to nasal ventilatory support. To this end, respiratory resistance (R_{rs}) measured by FOT at a frequency of 5 Hz and R_L measured simultaneously by means of an oesophageal balloon were compared. The study was conducted in patients with severe obstructive and chest wall restrictive disease in sitting and supine postures and subjected to different levels of nasal continuous positive airway pressure (CPAP). This procedure allowed the assessment of FOT at values of resistance covering the range typically found during noninvasive mechanical ventilation.

Methods

Patients

The study was carried out in 14 patients with severe chronic respiratory disease (table 1). Eight of the patients suffered from chronic obstructive pulmonary disease (COPD) and the other six patients presented a restrictive ventilatory defect due to chest wall disease. The patients were in a stable condition at the time of the study and were not premedicated 24 h prior to the test. The study was approved by the Ethics Committee of the Hospital and informed consent was obtained from each patient.

Measurements

The measurements were performed during application of CPAP by means of a conventional device (CP90; Taema, Airliquide, France), tubing and nasal mask. FOT was applied simultaneously to CPAP. To this end, a 5 Hz oscillation pressure (1.5 cmH_2O peak-to-peak) was applied at the nasal mask by means of a loudspeaker (JBL-800 GTI, 8-in subwoofer, 600 W; JBL, Vitoria, Spain) connected in parallel to the CPAP device (fig. 1). The rear part of the loudspeaker was attached to a 2-L closed chamber to withstand continuous positive pressures. Nasal pressure (P_n) was measured with a transducer (MP-45, ±20 cmH_2O; Validyne, Northridge, CA, USA). Nasal flow (V') was recorded with a Fleisch-type pneumotachograph (resistance of 0.35 $cmH_2O \cdot s \cdot L^{-1}$) connected to a differential transducer (MP-45, ±2 cmH_2O; Validyne). Oesophageal pressure (P_{oes}) was measured with a balloon (4 cm perimeter) filled with 1 mL of air and connected to a transducer (MP-45, ±50 cmH_2O Validyne) through a 90 cm long catheter (0.12 cm ID). After analogue low-pass filtering at 16 Hz (Butterworth type, 8-poles) to avoid aliasing, P_n, P_{oes} and V' were sampled at a rate of 100 Hz by a personal computer equipped with a data acquisition system (CODAS; DATAQ Instruments Inc, Akron, OH, USA).

Protocol

The oesophageal balloon was positioned and checked with the occlusion test as described by BAYDUR *et al.* [13].

Table 1. – Anthropometric and lung function data of patients

Patient No.	Sex	Age yrs	Weight kg	Height cm	FEV_1 L	FEV_1 % pred	FEV_1/FVC %	TLC L	TLC % pred
Obstructive patients									
1	M	63	66	162	0.85	29	34		
2	M	48	58	156	2.37	69	51		
3	M	76	60	163	0.56	21	40		
4	M	78	81	167	1.30	46	62		
5	M	71	65	174	1.08	32	37		
6	M	73	49	158	0.93	37	67		
7	M	71	73	166	1.01	34	32		
8	M	72	78	159	0.73	28	41		
Mean±SD		69±10	66±11	163±6	1.10±0.56	37±15	45±13		
Restrictive patients									
1	F	59	40	162	0.57	23	81	2.19	40
2	F	46	90	157	1.32	51	74	3.12	60
3	F	63	40	158	0.39	18	81	2.32	44
4	F	68	48	147	1.07	61	76	2.81	57
5	M	56	70	171	2.04	58	75	5.43	74
6	F	62	51	151	0.83	42	86	2.31	48
Mean±SD		59±8	57±20	158±8	1.00±0.59	42±18	79±5	3.03±1.22	54±12

FEV_1: forced expiratory volume in one second; FVC: forced vital capacity; M: male; F: female; TLC: total lung capacity measured by plethysmography.

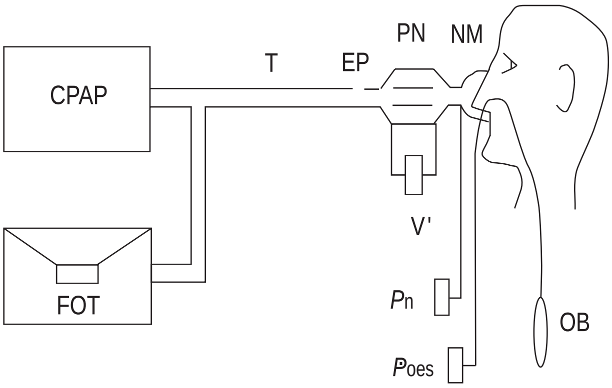

Fig. 1. – Diagram of the experimental setting used to perform the measurements by application of the forced oscillation technique (FOT) during continuous positive airway pressure (CPAP) nasal support. CPAP: Conventional CPAP device; FOT: loudspeaker-in-box system to apply 5 Hz forced oscillation; T: tubing; EP: exhalation port; PN: pneumotachograph; NM: nasal mask; OB: oesophageal balloon. Measured signals: nasal flow (V') and pressure (P_n) and oesophageal pressure (P_{oes}).

Before beginning the study, with the patient wearing all the equipment connected, the nasal mask was carefully fitted to minimize leaks. To this end, a CPAP of 5 cmH_2O was applied, the patient was required to stop breathing for a brief period and, if necessary, adjustments of the mask were made until leak with CPAP = 5 cmH_2O was <50 $mL \cdot s^{-1}$. Measurements on all patients were carried out in sitting and in supine postures, with the order of each posture selected at random. In the obstructive patients, for each posture the measurements were randomly performed at three different CPAP levels: 4, 8 and 12 cmH_2O. One of the obstructive patients was very uncomfortable in supine and would not perform the measurements in this posture. The protocol in the restrictive patients consisted of measurements in sitting and supine postures at a CPAP = 4 cmH_2O. Two of these patients were unable to tolerate measurements in supine posture. Each measuring condition (posture and CPAP) was maintained for a period of 10 min to allow patient's adaptation and then V', P_n and P_{oes} were recorded for a period of 2 min and stored for subsequent analysis.

Data analysis

To assess lung mechanics the signals P_n, P_{oes} and V' recorded in each patient and measuring condition were digitally low-pass filtered (8-pole Butterworth, cut-off frequency 2 Hz) to eliminate the 5 Hz FOT component. All of the data records were analysed to detect air leaks through the mask. To this end, the effective resistance of the leak was computed as the quotient between the mean P_n and the mean V' over a time period covering all the entire breathing cycles in the record. In all recordings except one, which was rejected (in one obstructive patient in supine at CPAP=12 cmH_2O), the actual leak resistance was >70 $cmH_2O \cdot s \cdot L^{-1}$. Transpulmonary pressure (P_{tp}) was obtained from the difference between P_n and P_{oes} and volume (V) was obtained by digital integration of V'. To compute the R_L and lung elastance (E_L) corresponding to each breathing cycle, the signals were fitted by least-square multiple linear regression to a simple resistance-elastance model: $P_{tp} = P_0 + E_L \cdot V + R_L \cdot V'$, where P_0 is the lung static recoil pressure at end-expiration ($V = 0$) [14]. To discard artefactual breathing cycles, *e.g.* those including oesophageal spasms, only the breathing cycles for which: 1) the fitting error of the model was <10%; and 2) the resulting R_L and E_L were positive, were accepted. According to these criteria ~25% of breathing cycles were rejected and, on average, 20 breathing cycles (SD=10) per patient and measuring condition were accepted for computing R_L and E_L. The mean and the coefficient of variation of R_L and E_L corresponding to the accepted breathing cycles in each patient and measuring condition were computed. FOT R_{rs} at 5 Hz was computed from the signals recorded at the nasal mask. P_n and V' were digitally high-pass filtered (8-pole Butterworth, cut-off frequency 2 Hz) to obtain the 5 Hz FOT components. Next, the Fourier coefficients of these signals were computed for each oscillation cycle and combined to obtain R_{rs} [15]. The R_{rs} values were then smoothed in the time domain using an 8-pole Butterworth low-pass filter with a cut-off frequency of 2 Hz and the few (~2%) outlying (>2 SD) R_{rs} values were rejected. The air enclosed in the mask in place (~50 mL) presented a shunt impedance at 5 Hz that was (~600 $cmH_2O \cdot s \cdot L^{-1}$) much higher than patient impedance and, consequently, no correction was applied for this shunt. Finally, the mean and coefficient of variation of R_{rs} were computed as the average of the values corresponding to the same breathing cycles for which R_L was computed for each patient and measuring condition.

Results concerning individual measurements are shown as mean±SEM and data concerning the populations of patients are given as mean±SD. Comparisons between resistance values were carried out with paired t-tests and the relationship between R_{rs} and R_L was assessed by linear correlation analysis.

Results

R_L obtained from the spontaneous breathing components of the recorded signals at the different CPAP values in sitting and supine postures are shown in table 2. Although not significant, R_L tended to decrease slightly as CPAP increased. As expected, in the obstructive patients R_L was significantly greater than in restrictive patients. Postural change from sitting to supine resulted in a significantly higher R_L in obstructive patients. In the obstructive patients E_L increased slightly with CPAP and rose from sitting to supine: 8.8±3.1, 8.4±4.0 and 10.4±4.6 $cmH_2O \cdot L^{-1}$ in sitting and 9.4±3.1, 9.2±4.4 and 10.8±4.1 $cmH_2O \cdot L^{-1}$ in supine, at 4, 8 and 12 cmH_2O of CPAP. As expected, in the restrictive patients E_L was significantly higher than in the obstructive patients (24.4±16.5 $cmH_2O \cdot L^{-1}$ in sitting and 27.5±10.3 $cmH_2O \cdot L^{-1}$ in supine).

R_{rs} measured by FOT is also shown in table 2. As illustrated by the scatter plot of R_{rs} *versus* R_L in all the patients at CPAP = 4 cmH_2O (fig. 2), these two resistance indices were highly correlated. Similar agreement between R_L and R_{rs} was found when modifying CPAP and body posture, as shown in table 2. The coefficient of linear correlation (r) between R_{rs} and R_L ranged 0.92–0.96 for both obstructive and restrictive patients in sitting and in supine postures. The linear regression resulted in an almost negligible constant term and in slopes that were

Table 2. – Patient lung and respiratory resistance

Patients	Posture	CPAP cmH_2O	*R*L $cmH_2O \cdot s \cdot L^{-1}$	*R*rs $cmH_2O \cdot s \cdot L^{-1}$	r	Constant $cmH_2O \cdot s \cdot L^{-1}$	Slope	CV(*R*L) %	CV(*R*rs) %
Obstructive	Sitting	4	14.4±6.8	11.5±5.9	0.92#	-0.01	0.80	9.1±5.0	7.5±2.3
		8	15.8±10.8	12.2±7.5	0.97*	1.52	0.67	6.4±3.8	10.5±5.0
		12	12.6±8.1	10.3±7.3	0.95*	0.59	0.74	11.7±9.6	9.2±2.2
	Supine	4	21.1±12.6	15.0±9.8	0.96*	-0.76	0.75	8.0±4.7	8.8±2.2
		8	19.1±11.6	15.6±9.8	0.98*	-0.10	0.82	6.1±2.5	7.4±2.0
		12	18.0±14.7	15.1±11.9	0.97*	1.05	0.78	9.1±5.3	10.5±2.8
Restrictive	Sitting	4	11.6±6.6	12.6±6.1	0.96*	2.18	0.89	19.3±11.4	8.8±3.9
	Supine	4	10.2±3.3	9.7±3.1	0.92#	0.98	0.86	15.5±11.8	7.5±1.9

Data are expressed as mean±SD. CPAP: continuous positive airway pressure; *R*L: lung resistance; *R*rs: respiratory resistance; r: linear correlation coefficient between *R*rs and *R*L. Constant and Slope: regression coefficients (*R*rs=Constant+Slope·*R*L). CV(*R*L) and CV(*R*rs): coefficients of variation in the measurements of *R*L and *R*rs, respectively. #: significant r at 1% level; *: significant r at 0.1% level.

0.67–0.82 in obstructive patients and slightly higher (0.86–0.89) in restrictive patients. Table 2 also shows that the variability (coefficient of variation between the respiratory cycles) in the measurement of *R*rs by FOT was similar (obstructive patients) or lower (restrictive patients) than the variability in the measurement of *R*L from the oesophageal balloon signal.

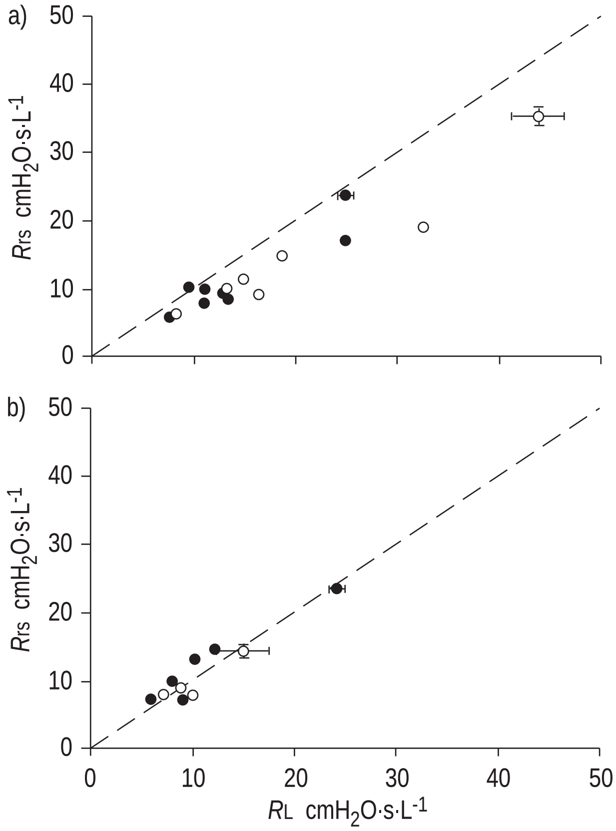

Fig. 2. – Respiratory resistance (*R*rs) noninvasively measured by forced oscillation *versus* lung resistance (*R*L) measured from the oesophageal pressure at continuous positive airway pressure (CPAP) = 4 cmH_2O in obstructive (a) and restrictive (b) patients, in sitting (●; a) n=8, b) n=6) and supine (○; a) n=7, b) n=4) postures. Data are mean±SEM (SEM intervals in most data are smaller than symbol size). The dashed line represents the identity line. One of the obstructive patients (a) and two of the restrictive patients (b) were unable to tolerate measurements in supine position

Discussion

The results found in this study show that respiratory resistance can be noninvasively assessed in patients with severe obstructive and restrictive disease who are breathing spontaneously through a nasal mask. The FOT was easily applicable when the patient was subjected to different levels of CPAP both in sitting and supine postures. The values of *R*rs obtained by applying a 5 Hz forced oscillation were close to and highly correlated with *R*L measured simultaneously, with similar measurement variability. However, the agreement between *R*rs and *R*L was in general better in the restrictive than in the obstructive patients (table 2, fig. 2).

To ascertain whether *R*rs measured by FOT was a reliable estimate of the patient's respiratory system resistance *R*rs was compared with *R*L measured by an oesophageal balloon, which is the well-established reference technique in spontaneously breathing patients. Nevertheless, it should be pointed out that these two resistance indices do not yield the same physiological information. Indeed, *R*rs is total respiratory resistance, *i.e.* lung plus chest wall resistance, at a frequency of 5 Hz and *R*L is lung resistance at the spontaneous breathing frequency. Nevertheless, the differences between *R*rs and *R*L in this application are expected to be small. On the one hand, *R*rs should be higher than *R*L due to chest wall resistance. However, in the current investigated patients the difference between *R*rs and *R*L should be small since chest wall resistance at 5 Hz makes a negligible contribution to total respiratory resistance [16–18]. On the other hand, *R*rs at 5 Hz should be lower than resistance at the spontaneous breathing frequency (*R*L) owing to the negative frequency dependence of resistance resulting from tissue viscoelasticity and airways inhomogeneity [19, 20]. In fact, the oscillation frequency of 5 Hz, which is in the lower limit of the conventional FOT frequencies, was selected to minimize, as much as possible, the influence of the frequency dependence of resistance due to viscoelasticity and inhomogeneity.

Besides the above mentioned possible differences between *R*L at the spontaneous breathing frequency and total respiratory resistance at a high frequency (5 Hz), discrepancies between measured *R*rs and *R*L could arise from using different measuring techniques. Evaluation of FOT when applied through a nasal mask in patients with markedly increased resistance was required since data in the literature do not provide evidence of the adequacy of the technique. By contrast, several studies where FOT was applied through a mouthpiece in patients have shown that the technique resulted in values of *R*rs which were considerably underestimated [7, 16]. This artefact, which is mainly due to the shunt of the extrathoracic upper airways [11], may be reduced if FOT is applied around the head by employing a special set-up [9]. However, such an FOT system is not applicable in routine noninvasive ventilation. To the authors' knowledge, FOT has been applied through a nasal mask in infants [21] and more recently in sleep studies, where the technique has been shown to be useful both for the diagnosis of sleep apnoea [11] and the titration of CPAP [10, 12]. The results found in this work when applying FOT through a nasal mask are probably due to the fact that when breathing through the nose the air pathway is substantially modified when compared with mouth breathing: the downwards and forwards movement of the soft palate associated with nose breathing isolates the wall-compliant oral cavity. Accordingly, the actual shunt of the extrathoracic upper airway, which is the main factor responsible for underestimation of *R*rs by FOT when breathing through the mouth, is reduced. Application of a forced oscillation frequency as low as 5 Hz contributed to the minimization of this potential artefact, which increases with frequency [8, 9].

It should be pointed out that the values of resistance measured from the oesophageal balloon and by FOT could also differ as a result of a possible air leak through the nose mask due to inadequate sealing. The role played by such a leak in the estimation of resistance is due to the fact that the leak pathway is placed in parallel between the impedance of the equipment (pneumotachograph, tubing and ventilator) and the impedance of the patient's respiratory system. In the FOT measurements *R*rs would be underestimated because part of the measured airflow would be lost through the leak. By contrast, in the measurements of *R*L this index would be overestimated since V' would be underestimated owing to the leak. However, the artefact due to a given air leak pathway is expected to be smaller in the measurement of *R*L than in that of *R*rs. Indeed, the impedance of the leak pathway would normally be much greater than the impedance of the equipment. By contrast, the impedance of the leak pathway could only be slightly higher than the respiratory impedance of a patient with a high degree of obstruction. For instance, an air leak of 0.1 $L \cdot s^{-1}$ when the mask pressure is 10 cmH_2O, which is not unusual in routine application of nasal ventilation, represents an effective leak resistance of 100 $cmH_2O \cdot s \cdot L^{-1}$. Consequently, if FOT was applied in these conditions to a patient with a very high resistance of 30 $cmH_2O \cdot s \cdot L^{-1}$ (fig. 2) the actual measured value of *R*rs would be underestimated by ~25%. Air leak is, therefore, a possible cause of *R*rs being lower than *R*L. It follows that especial attention should be paid to minimizing the air leaks as much as possible when FOT is applied to measure a patient's resistance. However, the presence of air leak can be easily detected and its resistance quantified from the recorded flow signal. A first method, which was the one used to adjust the mask at the beginning of the current study, consists of applying CPAP, asking the patient to stop breathing and then measuring the leak flow. A second method is based on the assumption that functional residual capacity is constant after several complete breathing cycles: leak flow is then computed from the mean flow measured over these cycles. This procedure, which was used to quantify the actual air leak corresponding to each FOT measurement, does not require the interruption of breathing and is, consequently, the most adequate for routine application during spontaneous breathing. This method, which may be affected by differences in inspired and expired gas conditions and by possible threshold effects and other nonlinearities in the leak pathway, should be viewed only as an indirect estimation of the magnitude of air leak.

The values of *R*L and *E*L found in the current patients were consistent with the data published in the literature [14, 22, 23]. Specifically, the obstructive patients were mainly characterized by a high *R*L and the restrictive patients exhibited a high *E*L. Moreover, in agreement with published data the authors did not find a substantial change in lung mechanics when the CPAP level was modified [22]. As expected in severe obstructive patients, changing body posture from sitting to supine resulted in a considerable increase in *R*L. In this regard, it should be mentioned that in some measuring conditions, particularly in supine, respiratory resistance was so high that the patient was dyspnoeic. In fact, in one of the patients it was not possible to carry out the measurements in the supine posture. These increases were induced in the mechanical load of the patient during the short period of the measurement to enlarge the range of resistance values. The procedure of modifying body posture allowed testing of the FOT over a wide range of resistance covering the values found in acute and chronic patients during noninvasive nasal ventilatory support [14, 16, 17].

In conclusion, this study found that forced oscillation technique applied through a nasal mask allowed the authors to noninvasively estimate respiratory resistance at different levels of continuous positive airway pressure (*i.e.* lung volume) without disturbing spontaneous breathing in patients with severe obstructive and restrictive disease. As forced oscillation technique provides automatic and real time resistance data [24], the use of this technique is of interest in clinical routine. Its potential clinical usefulness is enhanced by the fact that forced oscillation technique is a method which could be compatible with conventional ventilators with small modifications. Moreover, the technique could be incorporated as a function of the ventilator [25]. Measuring respiratory resistance at 5 Hz, which is an index dominated by airway resistance, allows an easy assessment of the degree of airway obstruction and, therefore, may provide information about the mechanical status and progress of the patient during noninvasive nasal ventilatory support. Future studies should address the question of whether this method could help to improve the matching between the ventilator and the patient by adapting the ventilation settings to the degree of patient obstruction.

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