# Forced oscillation total respiratory resistance and spontaneous breathing lung resistance in COPD patients

### R. Farré*, R. Peslin⁺, M. Rotger*, J.A. Barberá‡, D. Navajas*

*Forced oscillation total respiratory resistance and spontaneous breathing lung resistance in COPD patients. R. Farré, R. Peslin, M. Rotger, J.A. Barberá, D. Navajas. ©ERS Journals Ltd 1999.*

**ABSTRACT: Forced-oscillation total respiratory resistance ($R_{rs}$) has been shown to underestimate spontaneous breathing lung resistance ($R_{L,sb}$) in patients with airway obstruction, probably owing to upper airway shunting. The present study reinvestigates that relationship in seven severely obstructed chronic obstructive pulmonary disease patients using a technique that minimizes that artefact.**

$R_{rs}$ **at 8 and 16 Hz was computed for each successive forced oscillation cycle. Inspiratory and expiratory** $R_{L,sb}$ **were obtained by analysing transpulmonary pressure ($P_{tp}$) with a four-coefficient model, and compared to** $R_{rs}$ **over the same periods. "Instantaneous" values of** $R_{L,sb}$ **were also obtained by computing the dynamic component of** $P_{tp}$**, and compared to simultaneous values of** $R_{rs}$**.**

**In both respiratory phases, good agreement between** $R_{rs}$ **and** $R_{L,sb}$ **was observed up to** $R_{L,sb}$ **values of approximately 15 hPa·s$^{-1}$·L$^{-1}$ at 8 Hz and 10 hPa·s$^{-1}$·L$^{-1}$ at 16 Hz. Instantaneous** $R_{rs}$ **and** $R_{L,sb}$ **varied systematically during the respiratory cycle, exhibiting various amounts of flow- or volume-dependence in the seven patients; the amplitudes of their variations were significantly correlated, but** $R_{rs}$ **was much more flow-dependent than** $R_{L,sb}$ **in three patients. Also,** $R_{rs}$ **exceeded** $R_{L,sb}$ **at end-expiration in three instances, which could be related to expiratory flow limitation.**

**In conclusion, total respiratory resistance is reliable up to much higher levels of airway obstruction than previously thought, provided upper airway shunting is avoided.**
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Because it is strictly noninvasive and only requires passive cooperation from the subject, the measurement of total respiratory resistance ($R_{rs}$) by means of the forced oscillation technique (FOT) [1] is increasingly used to assess airway obstruction in patients. In contrast with forced expiration manoeuvres [2], the FOT does not modify bronchomotor tone [3], which makes it a method of choice for studying bronchial reactivity. To avoid interference from spontaneous breathing, the measurements are performed at frequencies at least one order of magnitude above normal breathing frequency. This confers to the method a time resolution good enough to follow changes of $R_{rs}$ through the respiratory cycle [4–6]. Conversely, a potential drawback of the high frequencies is that $R_{rs}$ may be substantially decreased by mechanical nonhomogeneity [7, 8] and airway wall shunting [9]. The reliability of $R_{rs}$ measurements by FOT for detecting airway obstruction and studying bronchial reactivity has been evaluated in a number of studies, by comparison to forced inspiration [10] or expiration indices [11, 12] and to resistance data obtained by other approaches [11 13, 14]. With some exceptions [13], these studies have shown that FOT had a sensitivity similar to that of the alternative methods.

In a few studies, however, FOT data have been compared to what is usually considered as the reference method in respiratory mechanics: the analysis of the relationship between transpulmonary pressure ($P_{tp}$), volume ($V$) and flow ($V'$) during spontaneous breathing. GRIMBY et al. [8] and NAGELS et al. [15] compared, in normal subjects and in chronic obstructive pulmonary disease (COPD) patients, lung resistance ($R_L$) obtained *via* FOT at 3–4 Hz to spontaneous breathing $R_L$ ($R_{L,sb}$). PHAGOO et al. [13] compared $R_{L,sb}$, $R_{rs}$ and other resistance indices in healthy humans before and after induced airway narrowing. In all of these studies, $R_{rs}$ was measured by applying the pressure input at the mouth, a condition in which $R_{rs}$ may be artefactually decreased, especially in obstructive patients, by the shunting of some of the measured flow through upper airway walls [16–18]. Therefore, to the authors knowledge, artefact free $R_{rs}$ and $R_{L,sb}$ have never been simultaneously measured and compared on the same respiratory cycles. The aim of this investigation was to better assess the reliability and clinical usefulness of FOT measurements at various frequencies for detecting airway obstruction in patients. For this, using a technique which minimizes the upper airway shunt, the relationship between simultaneously measured $R_{rs}$ and $R_{L,sb}$ in a group of COPD patients with a substantial degree of airway obstruction was studied in as much detail as possible. Besides comparing mean

inspiratory and expiratory resistances, the "instantaneous" values of $R_{L,sb}$ were computed to assess whether or not $R_{rs}$ variations during the respiratory cycle [4–6] were corroborated by $P_{tp}$ measurements.

## Materials and methods

The study was performed in seven patients with chronic airway obstruction diagnosed on the basis of clinical characteristics and the results of pulmonary function tests. The patients were in a stable condition at the time of the study and β-agonists were withheld $\geq 12$ h prior to the test. Their physical characteristics and lung function data are shown in table 1. The study was approved by the Ethics Committee of the hospital and informed consent was obtained from the patients.

### Measurements

Total respiratory impedance ($Z_{rs}$) was measured using the head generator technique [17] to minimize transmural pressure variations across the upper airway wall and the corresponding artefact [16, 17]. The generator consisted of a 40-L canopy placed around the head, sealed with a neck collar and connected to a 100-W loudspeaker. The latter was supplied with a computer-generated 2–32 Hz pseudorandom signal. The applied airway opening pressure ($P_{ao}$) was measured using a transducer (Honeywell 176; Honeywell Freeport, IL, USA), and gas flow ($V'$) using a Fleisch-II pneumatachograph (Sibel S.A., Barcelona, Spain) connected to a differential transducer (Honeywell 176). In addition, oesophageal pressure ($P_{oes}$) was measured with a balloon (4 cm perimeter) filled with 1 mL air and connected to a transducer (Honeywell 176PC/14) through a 90-cm-long catheter (0.12 cm internal diameter). The position of the balloon in the oesophagus was checked *via* the occlusion test of BAYDUR *et al.* [19]. $P_{tp}$ was obtained from the difference between $P_{ao}$ and $P_{oes}$. After low-pass filtering at 32 Hz to avoid aliasing, $P_{ao}$, $P_{oes}$ and $V'$ were sampled at a rate of 128 Hz for periods of 32 s using a personal computer system equipped with a 12-bit analogue–digital interface. Eight such records were collected in each patient over a period of 10 min.

### Data analysis

*Total respiratory resistance measurement.* Among the 16 frequency components in the forced oscillation signal, some had an integer number of data points per oscillation cycle (64 points at 2 Hz, 32 at 4 Hz, 16 at 8 Hz, eight at 16 Hz and four at 32 Hz). This permitted the computation of $R_{rs}$ on a cycle-by-cycle basis and the obtention, for the highest frequencies, of a much better time resolution than the basic repetition frequency of the excitation signal (2 Hz). Among these frequencies, 8 and 16 Hz were focused upon, since they combined a good time resolution and a large number of data points per cycle. The following analysis was made at each of these frequencies: $P_{ao}$ and $V'$ were first passed through a digital band-pass filter [20] centred on the frequency of interest, with a bandwidth of 4 Hz; the latter was found on simulated signals to be the best compromise for minimizing the influence of the other frequency components while permitting accurate following of fast changes in $R_{rs}$ (up to 1 Hz). Next, the Fourier coefficients of the signals were computed oscillation cycle by oscillation cycle and combined to obtain the real ($R_{rs}$) and imaginary parts ($X_{rs}$) of $Z_{rs}$. The data were corrected for the slight difference between the dynamic responses of the $P_{ao}$ and $V'$ pressure channels and for the 2.1 ms time constant of the pneumotachograph. Gas volume ($V$) was obtained by digital integration of $V'$, and the mean values of $V'$ and $V$ corresponding to each oscillation cycle were computed. Finally, the $R_{rs}$, $V$ and $V'$ data were smoothed in the time domain using an eight-pole Butterworth low-pass filter with a cut-off frequency of 2 Hz, and rejecting a few outlying $R_{rs}$ values (approximately 2% of cycles). Mean inspiratory and expiratory $R_{rs}$ were computed for each breathing cycle and for each record.

*Spontaneous breathing lung resistance measurement.* $P_{ao}$, $P_{oes}$ and $V'$ were first low-pass filtered (eight-pole Butterworth, cut-off frequency 2 Hz) to eliminate the FOT high frequency components. Then, the signals were fitted by means of least-squares multiple linear regression to the following model:

$$P_{ao} - P_{oes} = P0 + (E_L \times V + (R_{l,in} \times V'_{in}) + (R_{l,ex} \times V_{ex}) \quad (1)$$

where $P0$ is the lung static recoil pressure at end-expiration ($V=0$), $E_L$ is lung elastance, $R_{L,in}$ is inspiratory $R_{L,sb}$ and $R_{L,ex}$ is expiratory $R_{L,sb}$. $V'_{in}$ and $V'_{ex}$ are inspiratory and expiratory $V'$ respectively, and were set to zero during the expiratory and inspiratory phases, respectively. The fit was performed separately for each respiratory cycle. The above equation was preferred to the usual three-coefficient model ($P0$, $E_L$, $R_L$) because larger differences between inspiratory and expiratory resistances may be expected in patients than in normal subjects, and also because it permitted closer

Table 1. – Antropometric and lung function data of patients

| Subject No. | Sex | Age yrs | Height cm | Weight kg | FVC % pred | FEV1 % pred | TLC % pred | $C_{L,st}$ L·hPa$^{-1}$ |
|---|---|---|---|---|---|---|---|---|
| 1 | M | 77 | 167 | 97 | 51 | 56 | 113 | 0.093 |
| 2 | M | 60 | 165 | 67 | 78 | 25 | 167 | 0.112 |
| 3 | M | 38 | 176 | 66 | 40 | 28 | 107 | 0.041 |
| 4 | F | 48 | 163 | 78 | 85 | 42 | 146 | 0.146 |
| 5 | M | 64 | 175 | 84 | 52 | 30 | 108 | 0.118 |
| 6 | M | 69 | 169 | 73 | 70 | 38 | 93 | 0.064 |
| 7 | M | 59 | 171 | 75 | 59 | 27 | 112 | 0.292 |
| Mean | | 59 | 169 | 77 | 62 | 35 | 121 | 0.124 |
| SD | | 13 | 5 | 11 | 16 | 11 | 24 | 0.076 |

FVC: forced vital capacity; FEV1: forced expiratory volume in one second; TLC: total lung capacity (measured by plethysmography); $C_{L,st}$: static lung compliance; M: male; F: female.

Table 2. – Mean values of inspiratory and expiratory resistances derived from transpulmonary pressure and 8-Hz impedance measurements

| Subject No. | Measurements n | Inspiration | | | Expiration | | |
|---|---|---|---|---|---|---|---|
| | | $R_L$ hPa·L$^{-1}$·s$^{-1}$ | $R_{rs}$ hPa·L$^{-1}$·s$^{-1}$ | r | $R_L$ hPa·L$^{-1}$·s$^{-1}$ | $R_{rs}$ hPa·L$^{-1}$·s$^{-1}$ | r |
| 1 | 8 | 11.26±1.48 | 13.61±1.49[‡] | 0.952[+] | 13.23±1.97[#] | 14.91±1.46[#,‡] | 0.724[+] |
| 2 | 8 | 17.22±1.34 | 10.72±0.71[‡] | 0.506 | 20.78±1.96[#] | 13.50±1.33[#,‡] | 0.381 |
| 3 | 5 | 6.60±0.42 | 6.25±0.41 | 0.708 | 7.85±0.66[#] | 8.21±0.95 | 0.469 |
| 4 | 8 | 7.04±0.69 | 7.79±0.84[‡] | 0.666 | 9.61±1.54[#] | 10.08±2.01[#] | 0.896[+] |
| 5 | 7 | 9.39±0.67 | 11.15±1.31[‡] | 0.635 | 11.40±0.74[#] | 12.59±1.98[#] | 0.584 |
| 6 | 5 | 7.10±0.57 | 7.65±0.97 | 0.549 | 8.78±0.58[#] | 12.71±1.40[#,‡] | 0.672 |
| 7 | 8 | 11.87±1.55 | 12.20±0.60[‡] | 0.671 | 8.36±0.70[#] | 11.49±0.75[#,‡] | -0.379 |
| Total | 49 | 10.48±3.74 | 10.25±2.63 | 0.594 | 11.81±4.56[#] | 12.09±2.45[#] | 0.557[+] |

Data are presented as mean±SD. $R_L$: lung resistance; $R_{rs}$: real part of total respiratory impedance; r: coefficient of correlation between $R_L$ and $R_{rs}$. [+]: $p<0.05$ for $R_L$ versus $R_{rs}$ (r); [#]: $p<0.05$ for inspiratory versus expiratory values (paired t-test); [‡]: $p<0.05$ for $R_L$ versus $R_{rs}$ (paired t-test).

testing of the agreement between $R_{L,sb}$ and $R_{rs}$ data. To allow still closer comparison, instantaneous values of $R_{L,sb}$ ($R_{L,0}$), corresponding in time to each $R_{rs}$ value, were also computed. This was done by estimating the instantaneous resistive component of $P_{tp}$ ($P_{dyn}$) by subtracting from it the elastic terms using the values of $P_0$ and $E_L$ obtained on the same respiratory cycle:

$$P_{dyn}=(P_{ao}-P_{oes})-(P_0+E_L \times V) \qquad (2)$$

$P_{dyn}$ was averaged over the time periods corresponding to each 8 or 16 Hz forced oscillation cycle, and divided by the corresponding mean flow to obtain $R_{L,0}$. This was only done when the absolute value of the mean flow was >0.05 L·s$^{-1}$.

## Results

Among the eight sets of data recorded in each patient, eight were technically satisfactory in four patients, seven in one patient and five in two patients. Unsatisfactory measurements were caused by oesophageal contraction (three instances), irregular breathing (three instances) and a missing forced oscillation signal (one instance). All results are expressed as mean±SD. Equation 1 always gave a good fit to spontaneous breathing $P_{tp}$ with mean residuals ranging 3.7±0.3–7.0±0.4% of peak-to-peak $P_{tp}$. $E_L$ ranged 6.2± 0.9–10.8±0.7 hPa·L$^{-1}$ and its mean coefficient of variation between successive measurements was 11.2± 5.2%. The mean values of inspiratory and expiratory $R_L$ and $R_{rs}$ at 8 Hz in individual patients are shown in table 2. For both inspiration and expiration, $R_{rs}$ was similar to or >$R_L$ in all but one patient (subject 2), in whom significantly lower values were found using FOT. Mean $R_L$ and $R_{rs}$ for the whole group were not significantly different and were significantly correlated; the correlation was even better when the outlying patient was excluded (r=0.911 and 0.751 for inspiratory and expiratory data, respectively) (fig. 1a). In the patient who exhibited the greatest variability of resistance between repeated measurements (subject 1), significant correlations were also present between successive estimates of $R_L$ and $R_{rs}$ on both inspiration and expiration (table 2). $R_{L,ex}$ was significantly greater than $R_{L,in}$ in six patients, and significantly lower in one patient (table 2): differences in the same direction, although not always significant, were seen for $R_{rs}$, and the differences observed with the two approaches were

significantly correlated (r=0.621, p<0.001, for the 49 measurements).

Inspiratory and expiratory $R_{rs}$ decreased significantly from 8–16 Hz in all but one patient (subject 6). As a consequence, $R_{rs}$ at 16 Hz was, on average, slightly lower than $R_L$ (8.21±1.96 versus 10.48±3.74, p<0.001, on inspiration; 9.20±1.97 versus 11.81±4.56, p<0.001, on expiration); the correlations between the two estimates were, in general, a little less than at 8 Hz (r=0.788 and 0.634 for inspiration and expiration, respectively, when excluding the outlying patient) (fig. 1b).

Respiratory phasic variations of instantaneous resistances could be detected in all the records in five patients, and only occasionally emerged from the noise in the other two. For comparing $R_{rs}$ and $R_{L,0}$ variations, the records in which the periodic changes in $R_{rs}$ were the most prominent and regular were selected for each patient. From these records, using linear interpolation, block-averaged respiratory cycles of $V$, $V$, $P_{tp}$, $R_{rs}$ and $R_{L,0}$ were built with a time resolution corresponding approximately to that of the forced oscillation measurements (24 and 48 points per respiratory cycle for the 8 and 16 Hz data, respectively). The amplitudes of the variations in $R_{rs}$ decreased from 8 to 16 Hz in all instances (table 3). At 8 Hz, they were similar to those of $R_{L,0}$ in four patients, and substantially larger in the other three (table 3). $R_{rs}$ and $R_{L,0}$ were significantly correlated in all patients, but the correlations were in generally less at 16 than at 8 Hz (table 3). The patterns of variation were, for both $R_{rs}$ and $R_{L,0}$, fairly reproducible between successive measurements in an individual, but varied among patients, as illustrated in figure 2. In two patients (Nos. 1 and 2) both $R_{rs}$ and $R_{L,0}$ appeared largely related to absolute respiratory flow, being minimum at end-inspiration and expiration, and maximum in the vicinity of peak inspiratory and expiratory flow (fig. 2a); the flow dependence of 8-Hz $R_{rs}$ was similar to that of $R_{L,0}$ in one case (subject 2) and much larger in the other. In two patients (subjects 3 and 7, not shown), $R_{rs}$ and $R_{L,0}$ varied substantially with volume, being much higher at end-expiration than at end-inspiration, with almost no (subject 3) or less (subject 7) flow-dependence. The last three cases exhibited predominantly flow-dependent (subjects 5 and 6) or volume-dependent (subject 4) variations during the inspiratory phase, but were mostly characterized by an increasing discrepancy between $R_{rs}$ and $R_{L,0}$
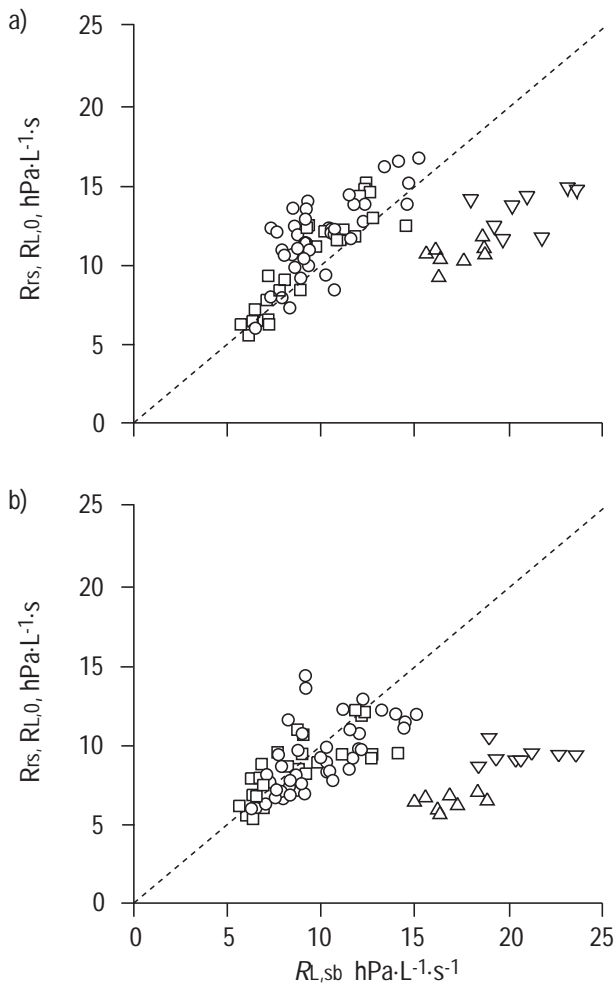
Fig. 1. – Relationship between forced oscillation total respiratory resistance ($R$rs), instantaneous values of spontaneous breathing lung resistance ($R$L,0,) and spontaneous breathing lung resistance ($R$L,sb) at: a) 8 Hz; and b) 16 Hz. o, m: mean inspiratory, expiratory resistance from a 32-s record; , -: inspiratory, expiratory resistance for an outlying patient (No. 2). The line of identity (- - -) is shown.

**Table 3. – Instantaneous lung and forced oscillation resistance in selected records**

| Subject No. | | 8 Hz | | 16 Hz | |
|---|---|---|---|---|---|
| | d$R$L,0 | d$R$rs | r | d$R$rs | r |
| 1 | 5.5 | 11.2 | 0.754 | 7.9 | 0.408 |
| 2 | 18.5 | 18.8 | 0.852 | 8.0 | 0.841 |
| 3 | 9.1 | 10.4 | 0.723 | 5.1 | 0.500 |
| 4 | 8.8 | 11.0 | 0.787 | 5.9 | 0.652 |
| 5 | 5.5 | 13.6 | 0.684 | 5.4 | 0.932 |
| 6 | 4.9 | 18.0 | 0.864 | 10.8 | 0.677 |
| 7 | 8.9 | 9.6 | 0.651 | 7.0 | 0.355 |
| Mean | 8.7 | 13.2 | | 7.2 | |
| SD | 4.7 | 3.8 | | 2.0 | |

d$R$L,0, d$R$rs: peak-to-peak amplitude of lung and forced oscillation total respiratory resistance in block-averaged cycles; measurement with the most prominent and regular phasic variations of total respiratory resistance ($R$rs) in each patient. +: $p<0.05$ for $R$rs *versus* instantaneous value of spontaneous breathing lung resistance ($R$L,0).

during the expiratory phase; while $R$L,0 decreased progressively after peak expiratory flow, $R$rs kept increasing until almost the end of the phase (fig. 2b). Except for the reduced amplitude (table 3), the phasic variations of 16-Hz $R$rs paralelled those at 8 Hz.

## Discussion

On the whole, this study demonstrated a strong relationship between 8-Hz $R$rs and $R$L,sb in COPD patients. Not only was the level of resistance similar in both approaches, except for one patient, but also the inspiratory-to-expiratory differences were well correlated, and the pattern of change in $R$rs and $R$L during the respiratory cycle was frequently similar. This was also largely true for 16-Hz $R$rs, although the correlations were usually less than at 8 Hz. As far as mean resistances are concerned, the present results are somewhat at variance with previous observations. GRIMBY *et al.* [8] and NAGELS *et al.* [15] compared values of $R$L obtained by FOT at 3–4 Hz to $R$L,sb in COPD patients; they observed that the FOT yielded systematically lower values when $R$L,sb exceeded approximately 5

hPa·L$^{-1}$·s$^{-1}$. In contrast, a linear relationship between 8-Hz $R$rs and $R$L,sb was observed in the present study, with a slope close to unity, up to resistances of 12 hPa·L$^{-1}$·s$^{-1}$ (fig. 1a); it was only when $R$L,sb was close to 20 hPa·L$^{-1}$·s$^{-1}$ (subject 2) that the 8-Hz $R$rs was clearly below the identity line; even at 16 Hz, $R$rs remained close to $R$L,sb up to values of 10 hPa·L$^{-1}$·s$^{-1}$. In other words, these data showed much less negative frequency-dependence of resistance in obstructive patients than previously observed. A minor reason for the discrepancy may be that FOT $R$rs which also includes the resistance of the chest wall ($R$w), was measured; the latter, however, has been shown to decrease with increasing frequency [21] and would rather enhance the negative frequency-dependence of $R$rs. Moreover, $R$w is in the order of only 1 hPa·L$^{-1}$·s$^{-1}$ in normal subjects [8, 21] and is not substantially increased in COPD patients [8]. More probably, the lower frequency dependence of FOT resistance in this study is due to the application of the pressure input around the head rather than at the mouth; this minimizes transmural pressure swings across extrathoracic airway walls, and the corresponding loss of flow through that parallel pathway [17]. The head generator technique has been shown to decrease substantially the negative frequency-dependence of $R$rs in obstructive patients [22]. Upper airway shunting may similarly explain, at least in part, the observation that the increase in $R$rs after induced bronchoconstriction in normal subjects is less than the increase in $R$L,sb [13]. The present observations, therefore, suggest that, provided the upper airway artefact is eliminated, FOT does not underestimate the level of airway obstruction up to resistance values of 10–15 hPa·L$^{-1}$·s$^{-1}$, depending on the oscillation frequency.

Another difference between this study and previous reports in which FOT $R$rs has been compared to $R$L,sb is the method used to compute $R$L,sb. GRIMBY *et al.* [8] obtained the resistive component of $P$tp by subtracting analogically from it a signal proportional to volume, and computed inspiratory resistance in the 0–0.5 L·s$^{-1}$ flow range; NAGELS *et al.* [15] and PHAGOO *et al.* [13] used an iso-volume method which provides a mean value for inspiratory and expiratory $R$L at the selected volume(s). In
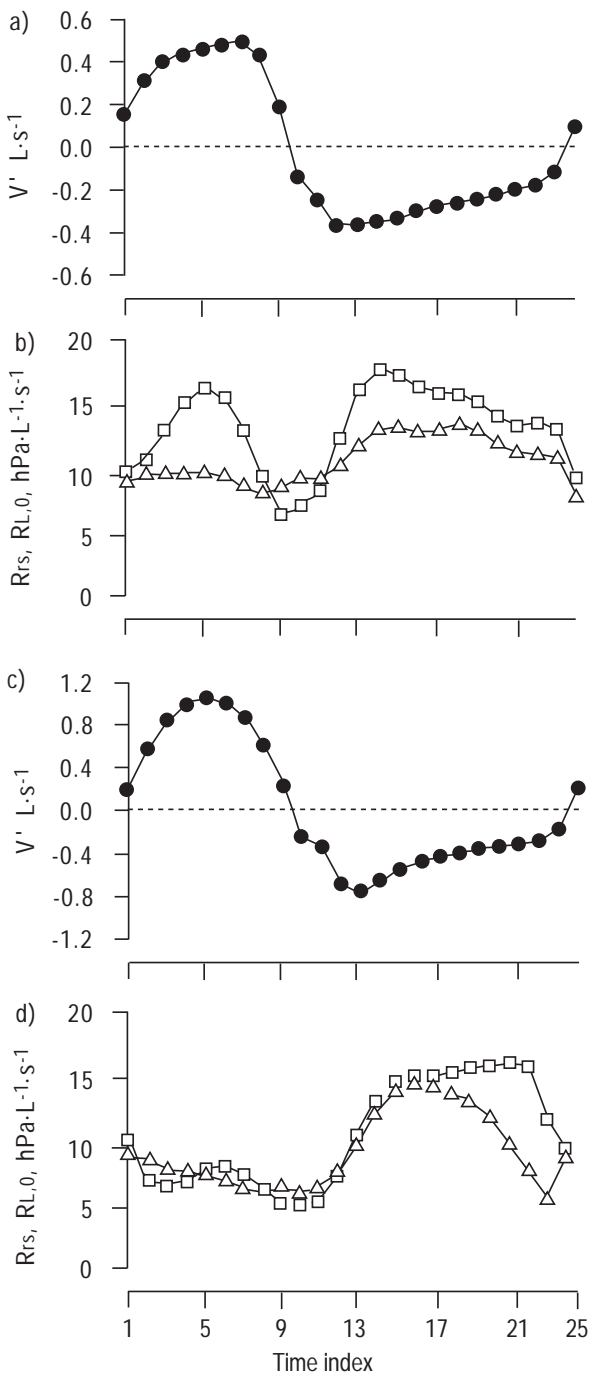
Fig. 2. – Block averaged cycles of: a and c) flow ($V'$, ●); and b and d) 8-Hz forced oscillation total respiratory resistance (Rrs, □) and instantaneous value of spontaneous breathing lung resistance ($R$L,0, △) in: a and b) subject 1; and c and d) subject 4, selected records. Time index: fraction of respiratory breathing cycle, 25 representing one breathing cycle.

tant to postulate that the resistance was the same in both phases. Surprisingly, however, the differences between $R$L,ex and $R$L,in, although significant in all patients (table 2), appeared to be moderate, ranging from -30–36%. It is the more remarkable that these differences were similar with the two measurement methods, and significantly correlated. The finding that resistance was, in general, greater during the expiratory phase is in agreement with previous findings [23, 24].

An interesting feature of the FOT is the possibility of computing $R$rs on time intervals as short as the reciprocal of the oscillation frequency. This feature has already been used in the past to study variations in resistance during the respiratory cycle [4–6]. In healthy subjects, it has been shown that $R$rs increases with increasing absolute flow, in agreement with R. Rohrer's equation [25], and decreases with increasing lung volume, as observed for plethysmographic airway resistance [26]; thus, $R$rs is maximum at peak inspiratory and expiratory flow, and minimum at end-inspiration [4–6]. Larger variations have been observed in patients with chronic airway obstruction [4, 5] and characteristic variations in $R$rs and $X$rs during expiratory flow limitation have been described in artificially ventilated patients with acute respiratory failure [27]. To the authors' knowledge, however, cyclical variations in $R$rs have not been compared with instantaneous $R$L derived from spontaneous breathing signals. Some differences between $R$rs and $R$L,0 may be expected for a number of reasons. Firstly, the dynamic component of $P$tp used to calculate $R$L,0 was computed using the values of $E$L and $P$0 obtained using the four-coefficient model described by equation 1. Thus, it is based upon the assumption that $E$L does not change over the tidal volume range and that it is correctly evaluated using this model. Actually, in patients with severe airway obstruction and, potentially, expiratory flow limitation, $E$L could either decrease during inspiration by reopening of dynamically closed airways or increase during inspiration owing to the shape of the static pressure-to-volume curve; mechanical inhomogeneity and lung viscoelasticity could also be responsible for variations in instantaneous $E$L during the respiratory cycle. A model including a volume-dependent elastance has been shown to explain the data in artificially ventilated patients significantly better [28]; it follows that the volume-dependence of $R$L,0 could as well be exaggerated as obscured by a volume-dependence of $E$L. Secondly, while $R$L,0 is the ratio of dynamic pressure to flow, $R$rs is the ratio of a change in pressure to a change in flow, $i.e.$ a differential resistance. One may predict that for a system described by R. Rohrer's equation ($P = (K_1 \times V')+ (K_2 \times V'^2)$), where $P$ is pressure, and $K_1$ and $K_2$ are constants, the differential resistance ($dP/dV'=K_1 + (2 \times K_2 \times V')$) would exhibit twice as much flow-dependence as the resistance ($P/V'= K_1 + (K_2 \times V')$). Thirdly, in the event of expiratory flow limitation, $R$L,0 would represent the total resistance of the lung, including the compressed airway segment, and be effort-dependent. In contrast, because the forced oscillation signal applied at the airway opening cannot pass through the flow-limiting segment, $R$rs is determined by the series impedance of the proximal (downstream) airways and the shunt impedance of the proximal airway walls [29].

In view of the above causes of differences, it is not surprising that, although significant correlations between

this study, the more general multiple linear regression method and a model allowing for differences between inspiratory and expiratory resistances were used. Indeed, several patients had a respiratory flow pattern suggestive of expiratory flow limitation, with an exponential decay in $V'$ after peak expiratory flow, and a rapid shift to inspiration at a time when expiratory flow was still substantial (fig. 2b). The authors were, therefore, reluc-

the variations in $R_{rs}$ and $R_{L,0}$ were observed in all subjects (table 3), at least in the records where the variations were most prominent, substantial differences were also observed. One of the most obvious is the flow-dependence of 8-Hz $R_{rs}$ which in several instances, was more than twice as great as that of $R_{L,0}$ even during the inspiratory phase, as illustrated in figure 2a. The authors have no satisfactory explanation for this difference, in excess of the predicted factor of two. Although phasic variations in tissue resistance [30] have been demonstrated in subjects breathing against mechanical loads, probably in relation to the increased activity of respiratory muscles, these variations did not reach the levels seen in this study. Unfortunately, in these severely obstructed patients, the signal/noise ratio of the high frequency components of the oesophageal pressure signal was not good enough to obtain reliable instantaneous values of chest wall impedance, and assess which part of the observed flow-dependence of $R_{rs}$ could be located in the chest wall. A second difference, illustrated in figure 2b and been in three patients, was the increasing discrepancy between $R_{rs}$ and $R_{L,0}$ in the second part of the expiratory phase. These patients were among those in whom the expiratory flow pattern clearly suggested expiratory flow-limitation, as described above. The authors therefore, hypothesized that the separation between the two resistance curves coincides with the occurrence of airway dynamic compression, when the peripheral lung would represent an almost infinite impedance for the forced oscillation signal. It could be argued, however, that the decrease in $R_{L,0}$ is not evocative of flow-limitation, and further work is needed to clarify the mechanism of this phenomenon.

Whatever their mechanism, important variations in $R_{rs}$ occur during the respiratory cycle. Such variations remain undetected when impedance is computed using data blocks of several seconds, as recommended for decreasing the noise [31], rather than oscillation cycle by oscillation cycle as carried out in this study. It is also usual to obtain an index of the variability of successive data blocks by computing the coherence function ($\gamma^2$) [16]. A value of $\gamma^2$ of close to unity is interpreted as indicating that the system is stationary, and that the noise level is low. It was wondered whether the large respiratory variations in $R_{rs}$ seen in the present study could be responsible for particularly low values of $\gamma^2$. The data were, therefore, reanalysed in the standard way, using data blocks of 0.5, 1, 2 and 4 s. The mean corresponding values of $\gamma^2$ at 8 Hz were $0.61\pm0.18$, $0.73\pm0.15$, $0.85\pm0.10$ and $0.93\pm0.06$, respectively. It therefore appears that when the duration of the block is similar to that of the respiratory period, the value of $\gamma^2$ may be close to 1 (above the usual threshold of 0.9 in 3 and 6 out of 7 patients for blocks of 2 and 4s, respectively), although the system is strongly nonstationary. This was to be expected since, theoretically, a variation in impedance with a period equal to the duration of the data blocks does not create any variability among the blocks.

In summary, in chronic obstructive pulmonary disease patients, good agreement between total respiratory resistance data freed from the upper airway artefact and spontaneous breathing lung resistance, up to severe levels of airway obstruction, was observed. This further validates the use of the forced oscillation technique for a number of clinical applications in patients, including the exploration of bronchial reactivity. It also suggests that the actual frequency dependence of resistance is less than previously thought in these patients. As a frequency dependence of total respiratory resistance may be a sign of diagnostic value, this stresses the need for properly eliminating the upper airway artefact. It may be achieved using a head generator, as carried out in this study, but the equipment is not widely available. The alternative is to apply pressure input *via* the mouthpiece and correct the data for the shunt impedance of upper airway walls, separately measured during Valsalva manoeuvres [16]. When only variations in airway obstruction are to be measured, a third possibility, is to compute the changes in respiratory admittance (the reciprocal of impedance), which are unaffected by the upper airway artefact [32]. Finally, potentially interesting similarities as well as differences requiring further investigation among the variations in total respiratory resistance and spontaneous breathing lung resistance during the respiratory cycle were found.

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