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G. A. Iotti
A. Braschi
J. X. Brunner
T. Smits
M. Olivei
A. Palo
R. Veronesi

Respiratory mechanics by least squares fitting in mechanically ventilated patients: applications during paralysis and during pressure support ventilation

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G. A. Iotti (✉) · A. Braschi · M. Olivei
A. Palo · R. Veronesi
Servizio di Anestesia e Rianimazione 1, Policlinico S. Matteo IRCCS, Pavia, Italy

J. X. Brunner · T. Smits
Hamilton Bonaduz AG, Bonaduz, Switzerland

Abstract *Objective:* To evaluate a least squares fitting technique for the purpose of measuring total respiratory compliance (C_{rs}) and resistance (R_{rs}) in patients submitted to partial ventilatory support, without the need for esophageal pressure measurement.
Design: Prospective, randomized study.
Setting: A general ICU of a University Hospital.
Patients. 11 patients in acute respiratory failure, intubated and assisted by pressure support ventilation (PSV).
Interventions: Patients were ventilated at 4 different levels of pressure support. At the end of the study, they were paralyzed for diagnostic reasons and submitted to volume controlled ventilation (CMV).
Measurements and results: A least squares fitting (LSF) method was applied to measure C_{rs} and R_{rs} at different levels of pressure support as well as in CMV. C_{rs} and R_{rs} calculated by the LSF method were compared to reference values which were obtained in PSV by measurement of esophageal pressure, and in CMV by the application of the constant flow, end-inspiratory occlusion method. Inspiratory activity was measured by $P_{0.1}$. In CMV, C_{rs} and R_{rs} measured by the LSF method are close to quasistatic compliance (-1.5 ± 1.5 ml/cmH_2O) and to the mean value of minimum and maximum end-inspiratory resistance ($+0.9 \pm 2.5$ cmH_2O/(l/s)). Applied during PSV, the LSF method leads to gross underestimation of R_{rs} (-10.4 ± 2.3 cmH_2O/(l/s)) and overestimation of C_{rs} ($+35.2 \pm 33$ ml/cmH_2O) whenever the set pressure support level is low and the activity of the respiratory muscles is high ($P_{0.1}$ was 4.6 ± 3.1 cmH_2O). However, satisfactory estimations of C_{rs} and R_{rs} by the LSF method were obtained at increased pressure support levels, resulting in a mean error of -0.4 ± 6 ml/cmH_2O and -2.8 ± 1.5 cmH_2O/(l/s), respectively. This condition was coincident with a $P_{0.1}$ of 1.6 ± 0.7 cmH_2O.
Conclusion: The LSF method allows non-invasive evaluation of respiratory mechanics during PSV, provided that a near-relaxation condition is obtained by means of an adequately increased pressure support level. The measurement of $P_{0.1}$ may be helpful for titrating the pressure support in order to obtain the condition of near-relaxation.

Key words Respiratory mechanics · Respiratory resistance · Respiratory compliance · Mechanical ventilation · Pressure support ventilation

Introduction

During pressure support ventilation (PSV), tidal inflation of the lungs is promoted by the synergistic action of the forces applied by the inspiratory muscles and by the mechanical ventilator. Both elements work against the total impedance of lungs and chest wall. Thus the quantification of impedance through measurements of total resistance (R_{rs}) and total compliance (C_{rs}) of the respiratory system can provide useful diagnostic information. In particular, during PSV these measurements can be helpful for titrating the ventilatory support and for deciding its discontinuation.

The assessment of total respiratory mechanics in mechanically ventilated patients is in widespread use and relatively simple to perform during paralysis and volume controlled ventilation (CMV) [1]. In this context, a number of techniques have been proposed to analyze airway pressure (P_{aw}), flow (V'_{aw}) and volume change (V_{aw}) for the measurement of C_{rs} and R_{rs}. Conventional methods require a constant inspiratory flow rate and an adequate end-inspiratory hold [2–5]. In the presence of dynamic pulmonary hyperinflation, an end-expiratory occlusion maneuver is also required for the measurement of intrinsic PEEP ($PEEP_i$), the latter to be taken into account for correct results [6]. As alternative to the conventional methods, a statistical approach has been suggested [7–9] and recently been applied more widely [10–14], referred to as the "Least Squares Fit" (LSF) method. The LSF method provides some advantages, since it allows the simultaneous measurement of R_{rs}, C_{rs} and total intrapulmonary PEEP ($PEEP_{tot}$) without the need for constant inspiratory flow rate, end-inspiratory hold, and end-expiratory occlusion [10–12]. These features of the LSF method allow its application to be extended to pressure preset ventilation modes such as pressure controlled ventilation (PCV).

During spontaneous breathing and PSV the theoretical basis for the application of the LSF method, and for this purpose, of any method based on the analysis of P_{aw}, V'_{aw} and V_{aw} is unsound because of the activity of the respiratory muscles. The additional measurement of esophageal pressure (Pes) is required, and the assessment of respiratory mechanics is limited to the lungs. However, increasing levels of pressure support are known to lead to progressive derecruitment of the respiratory muscles [15]. Exploiting this effect, a near-relaxation condition should be obtained at adequate levels of pressure support. The LSF method should be ideally suited for application in this context. In that case C_{rs} and R_{rs} could be directly and noninvasively evaluated from V'_{aw}, V_{aw} and P_{aw}, without the need for the measurement of Pes.

The aim of this study was to explore the LSF method and to identify conditions for its application during PSV.

Materials and methods

Patients

The study included 11 intubated patients, assisted by PSV for acute respiratory failure. The patients, 5 females and 6 males, were on average 60.5 ± 17.9 (range 21–76) years old. Patient data and pathology are listed in Table 1.

Protocol

Each patient was submitted to four different levels of pressure support. The baseline pressure support level (BPS) was set by the physician in charge for any given patient and was chosen according to clinical criteria. The pressure support level was then reduced by 5 cmH_2O (BPS−5), increased by 5 cmH_2O (BPS+5), and increased by 10 cmH_2O (BPS+10). Each pressure support level was applied in random order and for at least 30 minutes. Finally, each patient was sedated by diazepam, paralyzed by pancuronium bromide and submitted to volume controlled mechanical ventilation (CMV). CMV was administered by constant inspiratory flow rate, with a tidal volume (Vt) equal to 10 ml/kg, a respiratory rate titrated in order to maintain a constant end-tidal CO_2 concentration, an inflation time equal to 20% of the duration of the respiratory cycle (T_{tot}) and an end-inspiratory pause equal to 15% of T_{tot}. The inspiratory oxygen fraction (FiO_2) ranged from 0.4–0.65 and the

Table 1 Characteristics of patients and main pathology

Patient no.	Sex	Age (years)	Height (cm)	Weight (kg)	Pathology
1	M	72	172	80	Chest trauma
2	M	21	185	75	Head trauma sequelae
3	F	68	162	78	Chest trauma
4	F	64	165	70	Left ventricular failure
5	M	63	180	90	Vascular sepsis
6	M	59	160	50	ARDS
7	F	76	165	105	ARDS
8	M	69	175	55	Abdominal sepsis
9	F	31	168	65	Guillain Barré syndrome
10	F	69	168	61	ARDS
11	M	74	170	70	ARDS
Mean	6M/5F	60 ± 18	169 ± 9	72 ± 15	

PEEP level from 5–10 cmH_2O. The trigger level was set between –1 and –1.5 cmH_2O, choosing the minimum setting that prevented ventilator self-cycling. The settings of FiO_2, PEEP and trigger level were left unchanged during the whole study period. The study protocol was approved by the Ethics Committee of the Institution. At each level of pressure support and during CMV, measurements to determine the mechanics of the respiratory system were taken in steady state and analysed as described below.

Measurements

The patients were connected to a Hamilton AMADEUS ventilator (Hamilton Medical AG, Rhäzüns, Switzerland) and studied in semirecumbent position. V'_{aw} was measured with a Lilly-type pneumotachograph (Jäger PT-180) placed between the endotracheal tube and the Y-piece of the ventilator circuit, and connected to a ±12.5-cmH_2O differential pressure transducer (Micro Switch, Freeport, Illinois). P_{aw} was measured by a ±150-cmH_2O differential pressure transducer (Micro Switch). CO_2 concentration was measured by a mainstream analyzer (Novametrix Model 1260, Novametrix, Wallingford, CT), modified in order to decrease the rise time of the instrument down to 40 ms (10–90%). The dead space of the sensor head, including the CO_2 analysis cuvette, was less than 15 ml. Pes was measured by an esophageal balloon catheter (National Catheter Co., Argyle, NY) connected to a ±70-cmH_2O differential pressure transducer (Micro Switch) in all patients except for patients number 9, 10, and 11. The esophageal balloon was 9.5 cm long, had a perimeter of 3.6 cm, and was filled with 0.5 ml air. The position of the balloon in the esophagus was optimized by the occlusion test [16]. All signals were low pass filtered at 25 Hz (second order Bessel filter) and read into a personal computer by means of an analog-digital converter (DT2801-A, Data Translation, Marlboro, MA) at a rate of 60 samples per second and per channel. The flow signal was corrected for changes in gas composition and gas temperature [9]. The calibration of pressure signals was performed by a water manometer. The V'_{aw} signal was back calibrated from its time integral, after delivering a volume of 1550 ml by a syringe.

Analysis of respiratory mechanics

The analysis of pressure, flow and volume is based on a first order mechanical model of the respiratory system. In particular, it is assumed that total respiratory compliance (C_{rs}) and resistance (R_{rs}) remain constant throughout any given breath. Furthermore, it is assumed that the patient is entirely passive with respect to breathing activity. Equation 1 represents this relationship [17–19].

$$P_{aw}(t) = V_{aw}(t)/C_{rs} + V'_{aw}(t) \cdot R_{rs} + PEEP_{tot} \tag{1}$$

$V_{aw}(t)$ is the integral of V'_{aw} over time. $PEEP_{tot}$, total intrapulmonary end-expiratory pressure, is a constant and represents the sum of externally applied PEEP ($PEEP_e$) and intrinsic ($PEEP_i$), respectively expressing the static and the dynamic hyperinflation of the respiratory system [10]. In theory, only 3 equations are needed to solve for the 3 unknowns C_{rs}, R_{rs}, and $PEEP_{tot}$. However, since the primary signals V'aw and Paw are rather noisy, also C_{rs}, R_{rs} and $PEEP_{tot}$ would turn out to be imprecise. For this reason, all samples of any given breath are used. Since in our setting V'aw, Vaw, and Paw were measured 60 times per second, Eq. 1 could be formulated 60 times per second also. This series of equations was solved in a "least squares fit" sense and yielded one set of C_{rs}, R_{rs}, and $PEEP_{tot}$ per breath [7–9]. In statistical analysis, this procedure is well established and called multiple regression technique. This method was used to analyse respiratory mechanics at all levels of pressure support (BPS, BPS–5, BPS+5, and BPS+10) and during CMV, which gave one set of C^*_{rs}, R^*_{rs}, and $PEEP^*_{tot}$ for each condition. The asterisk (*) indicates that data were obtained by applying the LSF procedure to P_{aw}, V'_{aw} and V_{aw} only, without taking into account Pes. Therefore the interpretation of values marked by the asterisk requires information about the spontaneous breathing activity in each case, the assumption of respiratory muscle relaxation being fully given only during CMV. $PEEP^*_i$ was obtained by subtracting $PEEP_e$ from $PEEP^*_{tot}$.

In order to obtain reference measurements, the same type of analysis was applied to transpulmonary pressure, i.e. P_{aw} minus Pes, and to esophageal pressure. It then yielded lung compliance (C_L) and lung resistance (R_L), and chest wall compliance (C_W) and chest wall resistance (R_W) respectively. While C_L and R_L were obtained at all pressure support levels and CMV, the C_W and R_W could be measured only during CMV. The latter were assumed to remain constant throughout the study and used, together with the subsequently measured C_L and R_L, to calculate the reference values of C_{rs} and R_{rs} at each level of pressure support according to the following formulas:

$$R_{rs} = R_L + R_W \tag{2}$$

and

$$C_{rs} = 1/(1/C_L + 1/C_W) \tag{3}$$

For each level of pressure support and during CMV, reference $PEEP_{tot}$ was measured by the end-expiratory occlusion method [20]. The airway occlusion was performed by means of the end-expiratory hold function of the ventilator and maintained for at least 6 s. This time allowed to obtain an apparent plateau in P_{aw} both during CMV and PSV. Each value was an average of 3 maneuvers. Reference $PEEP_i$ was calculated as the difference between reference $PEEP_{tot}$ and $PEEP_e$.

For additional reference, the CMV breaths were analysed by the constant flow, end-inspiratory occlusion method [21], obtaining a conventional measurement of minimum inspiratory resistance (RiMin), maximum inspiratory resistance (RiMax), dynamic compliance (Cdyn), and quasistatic compliance (Cqs). For this purpose the end-inspiratory pause was analysed for P_1 and P_2 [21, 22]. The duration of the pause ranged from 0.6 to 0.8 s, and allowed to reach in its last part an apparent plateau in P_{aw}, that was read as P_2. The slow P_{aw} decay during the pause was backextrapolated to the time corresponding to peak airway pressure ($P_{aw,max}$), thus allowing the identification of P_1. The compliance and resistance variables were then calculated as follows, with Vi being the inhaled volume corresponding to P_2, and V'_i the inspiratory flow immediately preceding the occlusion:

$$Cdyn = Vi/(P_1 - PEEP_{tot}) \tag{4}$$

$$Cqs = Vi/(P_2 - PEEP_{tot}) \tag{5}$$

$$RiMin = (P_{aw,max} - P_1)/V'_i \tag{6}$$

$$RiMax = (P_{aw,max} - P_2)/V'_i \tag{7}$$

When the occlusion is obtained by standard ventilator valves as in this study, an overestimate of P_1 and P_2 results, due to the lack of immediate drop to zero of the inspiratory flow. This overestimate must be taken into account for the purpose of resistance calculation. A correction according to Kochi et al. [22] was used to compensate for this effect.

$P_{0.1}$ was measured by reading the P_{aw} drop after 100 ms during airway opening occlusion at the onset of inhalation, each value being an average of the data obtained from 3 maneuvers. The occlusion was performed by means of the end-expiratory hold function of the ventilator, as previously described by other authors [23], while P_{aw} was recorded by digital sampling at 60 Hz.

The collection of all data was made after at least 20 min of application of any given pressure support level in steady state, i.e. when the breathing pattern (tidal volume, frequency, end-tidal CO_2) was stable. Comparisons of variables between the different pressure support conditions were made by two-way analysis of variance, using the Friedman test. Differences between C_{rs} and C^*_{rs}, R_{rs} and R^*_{rs}, and $PEEP_i$ and $PEEP^*_i$ at various levels of pressure support were analyzed using the Wilcoxon signed rank test. Compliance and resistance results in CMV were compared using linear regression analysis. Also, bias and precision was calculated [24] and the differences were compared using the Wilcoxon signed rank test.

Results

Table 2 shows general effects of different pressure support levels on inspiratory activity and pattern. $P_{0.1}$, an index of inspiratory activity, was higher at the lower pressure support levels. Increasing levels of pressure support were associated with significant decreases of $P_{0.1}$ ($p = 0.0001$), while V_t, inspiratory time (T_i) and expiratory time (T_e) significantly increased ($p = 0.0001$). Mean inspiratory flow rate (V_t/T_i) did not significantly change ($p = 0.183$), while mean expiratory flow rate (V_t/T_e) significantly decreased ($p = 0.012$) with increasing pressure support levels. The setting of CMV that we chose resulted in a further increase of V_t, T_i and T_e. V_t/T_i was also increased by CMV, due to the presence of an end-inspiratory pause, with consequent reduction of the effective inflation time. In contrast, V_t/T_e was decreased due to the major increase of T_e.

The results of the LSF method at all pressure support levels are summarized in Table 3. R_{rs} and C_{rs} were

Table 2 Respiratory pattern and $P_{0.1}$ in all conditions investigated (11 patients)

	BPS-5		BPS		BPS + 5		BPS + 10		CMV	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
V_t	0.397	0.068	0.429	0.079	0.504	0.122	0.633	0.179	0.651	0.102
V_t/T_i	0.516	0.159	0.511	0.122	0.507	0.109	0.540	0.096	0.753	0.171
V_t/T_e	0.362	0.095	0.351	0.096	0.319	0.089	0.297	0.084	0.233	0.038
T_i	0.784	0.119	0.843	0.135	0.974	0.187	1.149	0.305	1.473	0.138
T_e	1.164	0.232	1.318	0.396	1.687	0.416	2.323	0.809	2.847	0.25
$P_{0.1}$	4.6	3.1	3.1	1.3	1.9	0.8	1.6	0.7	n.a	n.a

V_t tidal volume, *V_t/T_i* mean inspiratory flow, *V_t/T_e* mean expiratory flow, *T_i* inspiratory time, *T_e* expiratory time. Volumes are given in liter, flow in l/s, times in s, and pressures in cmH_2O. $P_{0.1}$ cannot be measured in paralyzed patients, therefore this entry is not applicable (n.a.) in CMV

Table 3 Respiratory mechanics in all conditions investigated, with mean differences between data obtained by the LSF procedure from P_{aw}, V'_{aw} and V_{aw} (asterisk *) and reference data

	BPS-5		BPS		BPS + 5		BPS + 10		CMV	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
C_L	36.97	11.83	39.88	15.34	46.21	18.33	52.46	24.79	54.04	23.25
C_W	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	114.3	55.34
C_{rs}	27.15	8.34	28.48	9.95	31.59	10.53	34.31	13.28	34.72	11.64
C^*_{rs}	62.31	40.18	41.86	21.73	36.13	13.23	33.94	12.04	34.72	11.64
R_L	8.50	2.78	8.76	3.05	10.57	2.64	11.91	2?.78	12.95	2.85
R_W	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	0.55	0.31
R_{rs}	9.05	2.93	9.32	3.18	11.13	2.83	12.46	2.97	13.51	3.05
R^*_{rs}	−1.32	2.92	2.55	2.41	6.66	3.01	9.66	2.58	13.51	3.05
$PEEP_i$	2.52	1.55	2.80	1.8	2.96	1.92	2.44	1.75	0.78	1.06
$PEEP^*_i$	−1.24	1.24	−0.62	0.87	0.85	1.32	1.34	1.35	0.47	0.89

	Mean	SD	p	Mean	SD	p	Mean	SD	p	Mean	SD	p	Mean	SD	p
$C^*_{rs} - C_{rs}$	35.2	33	0.01	13.4	14	0.02	4.5	7	0.05	−0.4	6	0.89	0	0	
$R^*_{rs} - R_{rs}$	−10.4	2.3	0.01	−6.8	1.2	0.01	−4.5	1.8	0.01	−2.8	1.5	0.01	0	0	
$PEEP^*_i - PEEP_i$	−3.8	1.5	0.003	−3.4	1.7	0.003	−2.1	1.9	0.004	−1.1	1.6	0.04	−0.3	1.1	0.48

Compliance and resistance data refer to patients 1 to 8. *p* values are results of Wilcoxon test. *C_L* lung compliance, *C_W* chest wall compliance, *C_{rs}* total compliance, *R_L* lung resistance, *R_W* chest wall resistance, *R_{rs}* total resistance, *$PEEP_i$* intrinsic PEEP. Compliance units are ml/cmH_2O, resistance units are $cmH_2O/(l/s)$ and $PEEP_i$ is given in cmH_2O. C_W and R_W could be measured only during CMV and thus the entries are not applicable (n.a.) in PSV calculated according to Eq. 2 and 3 respectively, while $PEEP_i$ was obtained by end-expiratory occlusion. C^*_{rs}, R^*_{rs} and $PEEP^*_i$ are the results of the LSF at various degrees of spontaneous activity. $PEEP_i$ and $PEEP^*_i$ were calculated by subtracting $PEEP_e$ from $PEEP_{tot}$ and $PEEP^*_{tot}$ respectively. When pressure support was low and spontaneous breathing activity high, C^*_{rs} grossly overestimated C_{rs}, and R^*_{rs} underestimated R_{rs}, the latter assuming even negative values in some instances. Also $PEEP^*_i$ was affected by spontaneous inspiratory activity, great underestimation of actual $PEEP_i$ being associated with low pressure support levels. Increasing levels of pressure support were associated with better agreement between C_{rs} and C^*_{rs}, and R_{rs} and R^*_{rs}, respectively. In particular at BPS+10, the maximum level explored, C^*_{rs} showed no significant difference from C_{rs}, and the difference between R^*_{rs} and R_{rs} was statistically significant but minor. Concerning $PEEP^*_i$, even at BPS+10 it was significantly lower than $PEEP_i$ obtained by end-expiratory occlusion. Table 3 also shows data during CMV, including C_W and R_W. In this condition C^*_{rs} and C_{rs}, as well R^*_{rs} and R_{rs}, were identical, as it is to be expected given the kind of analysis.

C_L and C_{rs} were generally and markedly decreased compared to values obtained after open heart surgery [9, 12], while resistance was only moderately increased and $PEEP_i$ was low. C_L and R_L, and consequently C_{rs} and R_{rs}, progressively increased with pressure support ($p = 0.058$ and $p = 0.0001$ respectively).

During paralysis and CMV, a comparison between total respiratory mechanics by LSF and by more conventional methods was made in all 11 patients. C^*_{rs}, obtained by the LSF method, was compared with Cqs and Cdyn. Linear regression analysis of these data is shown in Fig. 1. Even if both correlations are good ($Cdyn = 0.894 \cdot C^*_{rs} - 1.412$, $r^2 = 0.949$ and $Cqs = 0.914 \cdot C^*_{rs} + 4.203$, $r^2 = 0.981$), the analysis of bias and precision indicates a better agreement between C^*_{rs} and Cqs than between C^*_{rs} and Cdyn (Table 4). Figure 2 shows the relationship between R^*_{rs}, obtained by the LSF method, and resistances RiMin and RiMax. The results of the linear regression

Table 4 Mean and standard deviation of difference between LSF measurements and conventional methods of evaluation of respiratory mechanics during CMV (11 patients)

	Mean difference "bias"	SD "precision"	p
C^*_{rs} – Cdyn	4.77	2.32	0.003
C^*_{rs} – Cqs	–1.47	1.52	0.016
R^*_{rs} – RiMin	4.89	5.11	0.008
R^*_{rs} – RiMax	–3.05	2.03	0.003
R^*_{rs} – (RiMax + RiMin)/2	0.92	2.54	0.213

C_{rs} total compliance, *Cdyn* dynamic compliance, *Cqs* quasistatic compliance, *R_{rs}* total resistance, *RiMax* maximum inspiratory resistance, *RiMin* minimum inspiratory resistance. Compliance values are given in ml/cmH_2O and resistance values in $cmH_2O/(l/s)$. p values are result of Wilcoxon test

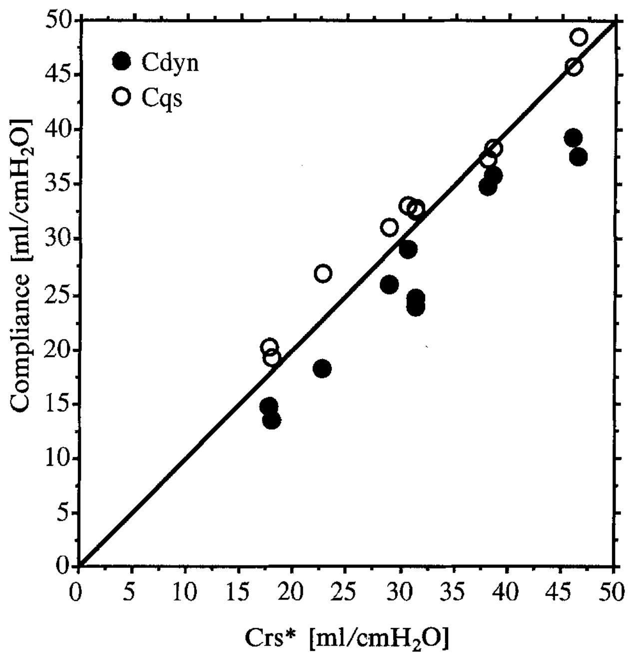

Fig. 1 Compliance measured with LSF (C^*_{rs}) during paralysis and CMV, plotted simultaneously against quasistatic (*Cqs*) and dynamic compliance (*Cdyn*). *Solid line* is line of identity, regression coefficients are given in the text

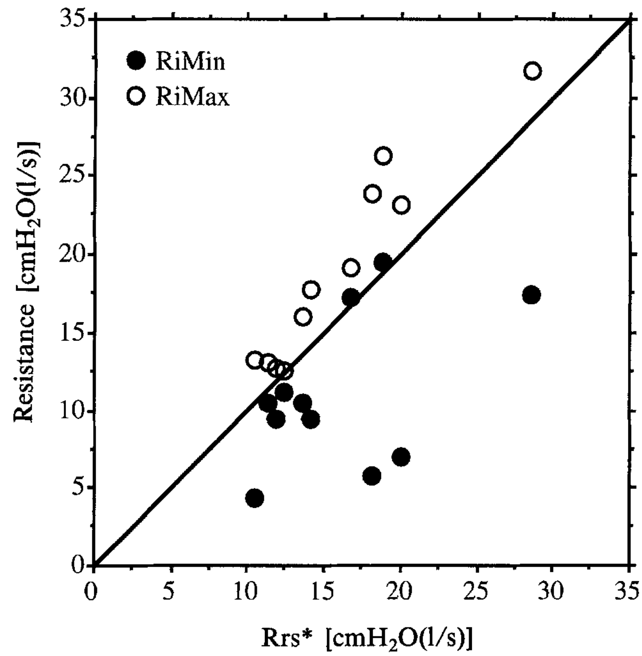

Fig. 2 Resistance measured with LSF (R^*_{rs}) during paralysis and CMV, plotted simultaneously against minimum (*RiMin*) and maximum inspiratory resistance (*RiMax*). *Solid line* is line of identity, regression coefficients are given in the text

analysis indicate a good agreement between R^*_{rs} and RiMax (RiMax = 1.171$\cdot R^*_{rs}$+0.326, $r^2 = 0.92$), while the correlation between R^*_{rs} and RiMin is poor (RiMin = 0.471$\cdot R^*_{rs}$+3.573, $r^2 = 0.251$). The error analysis confirms high bias and low precision in the comparison between R^*_{rs} and RiMin, while R^*_{rs} systematically underestimates RiMax, with an acceptable precision (Table 4). If R^*_{rs} is compared to the mean value of RiMax and RiMin, then the difference becomes nearly zero (Table 4). Even in the presence of good correlation and agreement, the statistical comparison indicates a significant difference between C^*_{rs} and both Cdyn and Cqs, as well as between R^*_{rs} and both RiMin and RiMax (Table 4). Concerning $PEEP_i$, neither a significant correlation nor a significant difference could be found between $PEEP_i$ obtained by the LSF method (0.475 ± 0.888 cmH_2O) and $PEEP_i$ obtained by the end-expiratory occlusion method (0.776 ± 1.058 cmH_2O).

Discussion

This study explored the LSF method to assess total respiratory mechanics at various degrees of spontaneous activity. The LSF approach was chosen because it requires neither special maneuvers nor particular flow patterns [12]. However, its application to measure R_{rs} and C_{rs} is restricted to passive patients, i.e. to patients without appreciable breathing activity. As reference values for R_{rs} and C_{rs}, we used the sum of lung and chest wall resistance according to Eq. 2, and the reciprocal sum of lung and chest wall compliance according to Eq. 3. Chest wall mechanics was measured during paralysis, and possible changes in the mechanical characteristics of the relaxed chest wall due to muscle tone were not taken into account.

Our results in CMV and paralysis confirm the observation of previous investigators [11–13] that the LSF method enables a simultaneous assessment of resistance and compliance, without any constraint concerning the ventilatory pattern. Only relaxation is required, while no particular inspiratory flow pattern and no end-inspiratory or end-expiratory occlusion maneuver are needed. The LSF method provides data of R_{rs} and C_{rs} which are weighted over the entire respiratory cycle. In contrast, the constant flow, end-inspiratory occlusion method provides a measurement of resistance which is limited to one particular flow at one level of volume, and a measurement of compliance based on two points, end of inspiration and end of expiration. For these reasons, perfect correspondence between the data obtained by the two methods is not to be expected. Nevertheless a good agreement was observed. In particular, C^*_{rs} was intermediate between Cdyn and Cqs, and agreed better with Cqs, while R^*_{rs} was intermediate between RiMin and RiMax, and agreed better with the mean of RiMax and RiMin. These finding are consistent with the results of Bertschmann et al. [11], who used Cqs and RiMax as reference values, and with the ones of Guttmann et al. [12], whose reference was represented by Cdyn and RiMin. Contrary to both the above-cited studies, however, the statistical analysis of our data shows a significant difference between each kind of measurement of compliance and resistance, indicating a specificity of each method. The different meaning of RiMin and RiMax, as well as that of Cdyn and Cqs, has been thoroughly discussed elsewhere [21, 22, 25]. Briefly, the inspiratory impedance can be partitioned into its elastic component, expressed by Cqs, intrinsic resistive component, expressed by RiMin, and stress adaptation plus pendelluft component. When an inspiratory hold is applied, stress adaptation and pendelluft generate the fall of P_{aw} from P_1 to P_2, which can be analysed as extra elastance, Cdyn being lower than Cqs, or more usually as the extra resistance ΔR resulting from the difference between RiMax and RiMin. The intermediate positions of C^*_{rs} between Cdyn and Cqs, and R^*_{rs} between RiMin and RiMax, may suggest that pendelluft and viscoelastic properties of the respiratory system are expressed partly as extra resistance and partly as extra elastance when the LSF method is applied. Concerning dynamic hyperinflation, $PEEP^*_i$ was lower than $PEEP_i$ in most cases. Although this result is in agreement with the literature [10], our data do not allow clear conclusions. In fact the range of values of $PEEP_i$ in our patients was too small and therefore provided no basis for a reasonable comparison with reference measurements.

Since the LSF method appears to work so well in CMV and eliminates the need for hold maneuvers, it was tempting to explore its applications during PSV. The LSF method was thus applied in conditions of lack of relaxation to assess total respiratory mechanics, yielding C^*_{rs} and R^*_{rs}. $P_{0.1}$ was used as an index of the inspiratory activity of the patient [26]. Our data show that, when patients actively inhale, the consequent distortion of the air flow profile is interpreted by the LSF method as an apparent increase of compliance, decrease of resistance, and decrease of total PEEP. By increasing the pressure support level, the respiratory drive of the patients is depressed, as shown by the decrease of both $P_{0.1}$ and respiratory rate. Near-relaxation of the respiratory muscles could thus be forced in the patients investigated, and a good match was found between R^*_{rs} and R_{rs}, and particularly between C^*_{rs} and C_{rs}, at high pressure support levels. In our patients near-relaxation was generally found with a pressure support level equal or less than 10 cmH_2O above the basal level. When this condition is met, C^*_{rs} and R^*_{rs} may be interpreted as the actual C_{rs} and R_{rs}, without the need for Pes measurement nor for paralysis and CMV. Our data suggest that this is not the case for the measurement of $PEEP_i$, whose real value was not reflected by $PEEP^*_i$ at any pressure support level.

Table 3 indicates that both C_{rs} and R_{rs} increase when pressure support is increased. The magnitude of these

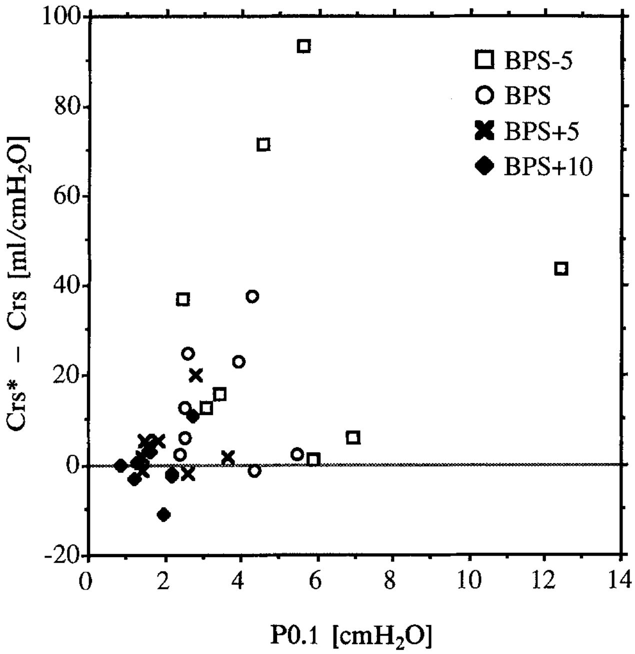

Fig. 3 Differences between C^*_{rs} and C_{rs} plotted against $P_{0.1}$. Results of all pressure support levels BPS−5, BPS, BPS+5, and BPS+10 are included

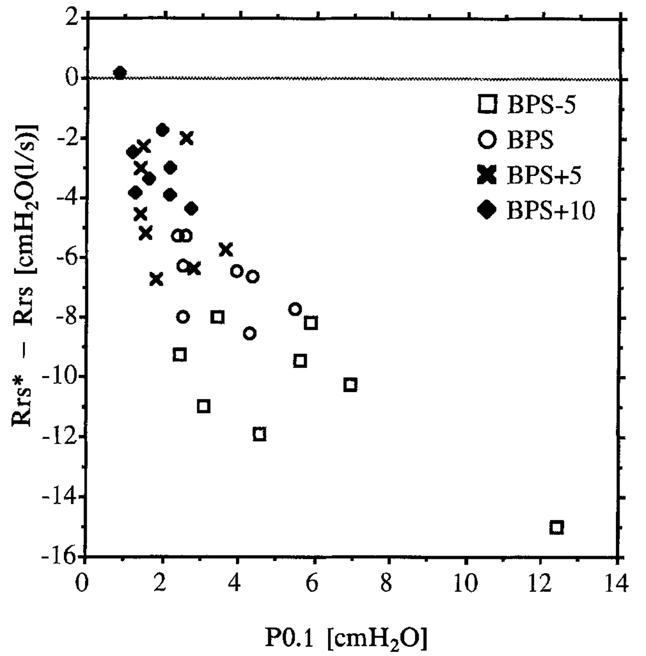

Fig. 4 Differences between R^*_{rs} and R_{rs} plotted against $P_{0.1}$. Results of all pressure support levels BPS−5, BPS, BPS+5, and BPS+10 are included

changes is limited, but the differences are statistically significant. This means that C_{rs} as well as R_{rs} may be slightly overestimated if measured at temporarily increased pressure support levels. In order to explain the observed changes of C_{rs} and R_{rs}, it must be pointed out that the rise of pressure support was associated with a moderate increase of tidal volume, no change in mean inspiratory flow and a moderate decrease of mean expiratory flow (Table 2), while $PEEP_i$ and hence the end-expiratory lung volume were unchanged (Table 3). A curvilinear pressure-volume relationship characterized by a lower compliance at lower lung volumes can explain the increase of C_{rs} with tidal volume and pressure support. The simultaneous increase of R_{rs} is more difficult to explain, since the associated changes of volume and flow predict a decrease of airway resistance [21, 22, 25]. Possible causes for the observed changes of R_{rs} include tissue viscoelastic properties, redistribution of ventilation, effects of spontaneous activity especially of diaphragmatic origin, and even redistribution of blood flow [5, 21, 22, 25]. Our data do not allow to distinguish between the different effects and further research is needed to elucidate the contribution of each factor. Only the increase of R_{rs} from the maximum level of PSV to CMV can be easily explained, if the concomitant increase of mean inspiratory flow and the marked non-linear characteristics of the endotracheal tube are considered.

Non-invasive assessment of respiratory mechanics by the LSF, near-relaxation method is made possible by a level of pressure support which is increased for the purpose of measurement. It is important, therefore, to have criteria for deciding when this level is adequate, i.e. when the near-relaxation condition is reached. In this study, $P_{0.1}$ was chosen as a simple index to test for respiratory activity. Figures 3 and 4 show the absolute error of C^*_{rs} and R^*_{rs} ($C^*_{rs} - C_{rs}$ and $R^*_{rs} - R_{rs}$, respectively) plotted against $P_{0.1}$. At high $P_{0.1}$ the associated error in C^*_{rs} and R^*_{rs} measurement is high, while it approaches zero with low values of $P_{0.1}$. Figures 3 and 4 suggest that $P_{0.1}$ can be used as a guide for the interpretation of C^*_{rs} and R^*_{rs} at any given pressure support level.

In conclusion, the LSF method provides data of resistance and compliance comparable with those obtained by the conventional constant flow, end-inspiratory occlusion method. However, its field of application is wider. In particular, it may allow a non-invasive assessment of respiratory mechanics during PSV, provided that the pressure support level is high enough to effect near-relaxation of the respiratory muscles. Near-relaxation can be expected when $P_{0.1}$ is equal or lower than 1.5 cmH_2O, provided that conditions like severe airway obstruction are excluded, that may prevent $P_{0.1}$ to adequately reflect the neural drive. The data presented in this study suggest that, whatever the current pressure support level of a patient is, an increase of 10 to 15 cmH_2O maximum will result in sufficient depression of the inspiratory activity to allow the application of the LSF method, thus providing useful clinical information.

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