Single-breath method for assessing the viscoelastic properties of the respiratory system

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ABSTRACT: In order to explain the time dependency of resistance and elastance of the respiratory system, a linear viscoelastic model (Maxwell body) has been proposed.

In this model the maximal viscoelastic pressure ($P_{\text{visc,max}}$) developed within the tissues of the lung and chest wall at the end of a constant-flow (V') inflation of a given time (t) is given by: $P_{\text{visc,max}} = R_2 V' (1 - e^{-t/\tau_2})$, where R_2 and τ_2 are, respectively, the resistance and time constant of the Maxwell body. After rapid airway occlusion at t_1 , tracheal pressure (P_{tr}) decays according to the following function: $P_{\text{tr}}(t) = P_{\text{visc}}(t) + P_{\text{rs,st}} = P_{\text{visc,max}} e^{-(t-t_1)/\tau_2} + P_{\text{rs,st}}$, where t_{occ} is time after occlusion and $P_{\text{rs,st}}$ is static re-coil pressure of the respiratory system. By fitting P_{tr} after occlusion to this equation, τ_2 and $P_{\text{visc,max}}$ are obtained. Using these values, together with the V' and t_1 pertaining to the constant-flow inflation preceding the occlusion, R_2 can be calculated from the former equation. Thus, from a single breath, the constants τ_2 , R_2 and E_2 (R_2/τ_2) can be obtained.

This method was used in 10 normal anaesthetized, paralysed, mechanically ventilated subjects and six patients with acute lung injury.

The results were reproducible in repeated tests and similar to those obtained from the same subjects and patients with the time-consuming isoflow, multiple-breath method described previously.

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In 1955, MOUNT [1] proposed a linear viscoelastic model in order to explain the time dependency of the resistance and elastance observed in normal rat lungs. In this model, the viscoelastic properties can be characterized by two parameters, the theoretical maximal viscoelastic resistance (R_2) and elastance (E_2). A third useful variable, the time constant (τ_2) can also be obtained as R_2/E_2 [2]. Using the technique of rapid airway occlusion (RAO) during constant-flow inflation, it has been possible to determine the values of these viscoelastic constants for the lung, chest wall and total respiratory system in normal mechanically ventilated humans [3–5] and experimental animals [2, 6] based on either one of the following functions:

$$P_{\text{visc}}(t) = R_2 V' (1 - e^{-t/\tau_2}) \quad (1)$$

$$R_{\text{visc}}(t) = P_{\text{visc}}(t)/V' = R_2 (1 - e^{-t/\tau_2}) \quad (2)$$

where P_{visc} is viscoelastic pressure within the lung and chest wall and $P_{\text{visc}}(t)$ in Equation 1 represents the viscoelastic pressure dissipation within the lung, chest wall or both during constant-flow (V') inflation started from the relaxed volume of the respiratory system, and t is any given time during lung inflation. Equation 2, where R_{visc} is viscoelastic resistance, is obtained by dividing both sides of Equation 1 by V' [3]. This analysis, however, is time consuming and technically complex because it requires

either a series of isovolume inflations with different inspiratory flows, or multiple isoflow inflations of different volumes [3, 6]. As a result, the above analysis has been used only in a limited number of studies on normal subjects [3–5] and patients [7–9].

In the present investigation, a single-breath method to assess the viscoelastic constants of the respiratory system is described and results obtained in normal anaesthetized paralysed subjects and in patients with acute lung injury (ALI) are provided. These data are compared with those obtained on the same subjects and patients using the method of multiple isoflow inflations of different volumes.

Theory

Figure 1 shows a representative record of tracheal pressure (P_{tr}) obtained in a normal anaesthetized paralysed subject during constant-flow inflation with RAO performed at an inspiratory (inflation) time (t_i) of 0.9 s. End-inspiratory airway occlusion is characterized by a rapid initial drop in P_{tr} ($P_{\text{tr,max}} - P_1$ where $P_{\text{tr,max}}$ is maximal P_{tr} and P_1 is the pressure that $P_{\text{tr,max}}$ falls to) followed by a slow decay to an apparent plateau pressure. The latter reflects the static end-inspiratory elastic recoil pressure of the respiratory system ($P_{\text{rs,st}}$) whilst $P_{\text{tr,max}} - P_1$ represents the interruptor pressure, which mostly reflects flow-dependent pressure dissipations within the airways, although there is also a

Fig. 1. — Time course of tracheal pressure (P_{tr}) during constant-flow inflation and end-inspiratory airway occlusion. After end-inspiratory airway occlusion, there is an immediate drop in pressure from maximal P_{tr} ($P_{tr,max}$) to P_1 followed by a slow decay to a plateau value that represents the static elastic recoil pressure of the respiratory system ($P_{rs,st}$). —: curve fitted according to Equation 5; - - - : constant $P_{rs,st}$ in Equation 5.

small component due to the Newtonian resistance of the chest wall [10, 11]. By contrast, the difference between P_1 and $P_{rs,st}$ reflects P_{visc} . At the time of occlusion (*i.e.* t_1), P_{visc} is maximal and henceforth will be labelled $P_{visc,max}$. From Equation 1, $P_{visc,max}$ is given by

$$P_{visc,max} = R_2 V'(1 - e^{-t_1/\tau_2}) \quad (3)$$

According to the viscoelastic model of MOUNT [1], P_{visc} during the end-inspiratory occlusion, should decay according to the following function:

$$P_{visc}(t) = P_{visc,max} e^{-t_{occ}/\tau_2} \quad (4)$$

where t_{occ} is time after RAO. The time course of P_{tr} during the end-inspiratory occlusion is obtained by adding $P_{rs,st}$ to both sides of Equation 4:

$$P_{tr}(t) = P_{visc}(t) + P_{rs,st} = P_{visc,max} e^{-t_{occ}/\tau_2} + P_{rs,st} \quad (5)$$

where, at $t=0$, $P_{tr} = P_{visc,max} + P_{rs,st} = P_1$ (fig. 1).

By fitting the experimental time course of the decay in P_{tr} during end-inspiratory occlusion to Equation 5, the values of $P_{visc,max}$, τ_2 and $P_{rs,st}$ can be derived. Using the values of $P_{visc,max}$ and τ_2 , together with those of V' and t_1 pertaining to the corresponding constant-flow lung inflation, the value of R_2 can be computed from Equation 3. Next, E_2 is obtained by $E_2 = R_2/\tau_2$. Thus, during a single constant-flow inflation followed by an end-inspiratory pause with occluded airway (single-breath method), the viscoelastic constants of the respiratory system can be obtained.

Materials and methods

Ten subjects (seven males) undergoing general anaesthesia (premedication: diazepam, 7.5 mg *per os*; anaesthesia: propofol, 2 mg·kg⁻¹ *i.v.*; muscle paralysis: succinylcholine, 1 mg·kg⁻¹ *i.v.*; maintenance: continuous infusion of propofol, 8–12 mg·kg⁻¹·h⁻¹, and vecuronium, 0.15 mg·kg⁻¹·h⁻¹) for minor lower abdominal or limb surgery were studied before skin incision. None had a history or clinical evi-

dence of cardiopulmonary disease. Their mean ($\pm$ SD) age, weight and height were 29 $\pm$ 8 yrs, 71 $\pm$ 13 kg and 175 $\pm$ 8 cm, respectively. In all subjects the vital capacity and forced expiratory volume in one second (FEV₁) were within $\pm$ 10% of the predicted values [12].

Six patients with ALI (arterial oxygen tension (P_{a,O_2})/inspiratory oxygen fraction (F_{I,O_2}) <300 mmHg and bilateral infiltrates on the chest radiograph) [13], who were admitted to the intensive care unit, were also studied. In all of them the measurements were performed after haemodynamic stabilization had been achieved for 1 day. The patients were sedated (propofol, 4 mg·kg⁻¹·h⁻¹) and paralysed (vecuronium 0.15 mg·kg⁻¹·h⁻¹). The anthropometric characteristics of the ALI patients are provided in table 1. None had a history or clinical evidence of either chronic lung disease, cardiogenic pulmonary oedema or active cardiac disease. The patients were studied at zero end-expiratory airway pressure (ZEEP). All subjects, in supine position, were intubated with a Rush cuffed endotracheal tube (7.5–8.0 mm i.d.) and ventilated with constant-inflation, flow-controlled ventilation by means of a Servo Ventilator 900C (Siemens-Elema AB, Solna, Sweden). RAOs were performed using a solenoid valve (Airmatic SV; Airmatic-Allied, Wilmington, OH, USA) placed next to the oral end of the endotracheal tube. The solenoid valve has a closing time of 11 ms (as measured at the Electronics Laboratory, Dept of Energetics, Faculty of Engineering, Trieste, Italy, with an accelerometer (Bruel & Kjaer 4332; Bruel & Kjaer Italiana, Milan, Italy) and a current probe (AC-DC Fluke Y8100; Fluke Corporation, Everett, WA, USA) connected to a rapid recorder (Hioki 8830; Hioki E.E. Corporation, Nagano, Japan)). Flow was measured with a heated Jäger Baby pneumotachograph (Würzburg, Germany) with a $\pm$ 3 L·s⁻¹ linearity range. The pneumotachograph was inserted between the endotracheal tube and the solenoid valve, and was connected to a Validyne MP-45 pressure transducer ($\pm$ 2 cmH₂O, Northridge, CA, USA) and to a carrier amplifier (13–4615–35; Gould, Cleveland, OH, USA). Tracheal pressure was measured, via a polyethylene catheter protruding 2–3 cm beyond the tracheal end of the endotracheal tube with a piezoresistive differential pressure transducer (Microswitch 142PC05D; Honeywell, Scarborough, Ontario, Canada). The tracheal catheter (1.5 mm i.d.) had six side holes at its distal end and an occluded tip. The system used to measure P_{tr} had no appreciable phase shift and its response was flat up to 20 Hz. The overall dead space of the measuring equipment (excluding the endotracheal tube) was 35 mL. The

Table 1. — Characteristics and diagnosis of patients with acute lung injury

Patient No.	Sex	Height cm	Weight kg	Age yrs	Diagnosis	$P_{a,O_2}/F_{I,O_2}$ mmHg
1	M	172	81	37	Sepsis	145
2	M	196	92	35	Pancreatitis	135
3	F	162	69	66	Sepsis	100
4	M	164	75	71	Multiple injury	125
5	F	166	61	59	Sepsis	210
6	M	168	73	43	Burns	160

M: male; F: female; P_{a,O_2} : arterial oxygen tension; F_{I,O_2} : inspiratory oxygen fraction. (1 mmHg=0.133 kPa.)

resistance offered by this equipment was $8 \text{ cmH}_2\text{O}\cdot\text{L}^{-1}\cdot\text{s}^{-1}$ at a V' of $1 \text{ L}\cdot\text{s}^{-1}$. Flow and P_{Tr} signals were fed through a 12-bit analogue-to-digital converter (Data Translation DT-2801A; Data Translation, Marlboro, MD, USA) into an IBM-compatible computer. Sampling frequency was established at 200 Hz. Volume was obtained by numerical integration of the flow signal. All data were analysed using ANADAT data analysis software (RHT-InfoData, Montreal, Quebec, Canada). Great care was taken to avoid leaks around the tracheal cuff and in the equipment. In all patients, the electrocardiogram and arterial blood pressure were monitored continuously, along with peripheral oxygen saturation and end-tidal carbon dioxide tension (Ohmeda 5250 RGM; Louisville, CO, USA). An anaesthetist who was not involved in the experiment was present to provide patient care.

Experimental procedure and data analysis: baseline conditions

Normal subjects were ventilated on ZEEP ($F_{\text{I},\text{O}_2} = 0.4$) with a V' of $0.50 \pm 0.01 \text{ L}\cdot\text{s}^{-1}$, a τ of $0.98 \pm 0.08 \text{ s}$ and a respiratory frequency (f_{R}) of $15\text{--}16 \text{ breaths}\cdot\text{min}^{-1}$, except for subject No. 9. This patient weighed 100 kg and had a body weight that was 24.6 kg (33%) above the desirable weight predicted on the basis of sex, age and height (body mass index of $29.8 \text{ kg}\cdot\text{m}^{-2}$) [14]. In this patient, τ was set at 1.38 s and f_{R} at $11 \text{ breaths}\cdot\text{min}^{-1}$. With these settings, there was normocapnia in all patients and intrinsic positive end-expiratory pressure (PEEP_i) was absent, as indicated by the fact that each inflation was preceded by a period of zero flow (end-expiratory pause) and that during end-expiratory airway occlusions P_{Tr} was zero. The baseline tidal volume (V_{T}) amounted to $6.6 \pm 0.6 \text{ mL}\cdot\text{kg}^{-1}$. During the experiments, the ALI group was ventilated on ZEEP ($F_{\text{I},\text{O}_2} = 0.5$) with a V' of $0.71 \pm 0.15 \text{ L}\cdot\text{s}^{-1}$, a τ of $0.92 \pm 0.24 \text{ s}$ and an f_{R} of $16\text{--}18 \text{ breaths}\cdot\text{min}^{-1}$. The mean value ($\pm \text{SD}$) of PEEP_i was $3.0 \pm 2.1 \text{ cmH}_2\text{O}$.

Single-breath method

End-tidal inspiratory occlusions, which lasted for 4 s, were obtained with the solenoid valve triggered by the Servo Ventilator. The volume loss due to the continuous gas exchange had a negligible impact on P_{Tr} . Data collection started during an end-expiratory occlusion for assessment of PEEP_i. After an end-expiratory occlusion, five recovery breaths at baseline ventilatory settings ensued; they were followed by an end-inspiratory occlusion. All measurements were repeated three times under the same experimental conditions. Between each test V' , V_{T} and P_{Tr} were allowed to return to baseline values.

As shown in figure 1, the end-inspiratory occlusions were followed by an initial rapid drop of P_{Tr} to P_1 and by a subsequent gradual decrease to an apparent plateau reflecting $P_{\text{Rs},\text{st}}$. The values of $P_{\text{Visc},\text{max}}$, $P_{\text{Rs},\text{st}}$ and τ_2 were obtained by computer fitting of the experimental data of P_{Tr} obtained during end-inspiratory occlusion to Equation 5. In this analysis, curve fitting started about 25 ms after occlusion to avoid the initial post-occlusion oscillations in P_{Tr} [15] and was carried out throughout the remainder of the 4 s. P_1 was obtained by back extrapolation of these exponential functions [15], whilst $P_{\text{Rs},\text{st}}$ was taken as P_{Tr} 4 s after the onset of occlusion.

In this analysis, the onset of the occluded inspiration corresponds to the end of the preceding constant V' inflation obtained with a given τ . Accordingly, the difference $P_1 - P_{\text{Rs},\text{st}}$ should correspond to the value of the P_{Visc} at τ ($P_{\text{Visc},\text{max}}$). Using this value and the corresponding τ_2 , together with the experimental values of V' and τ , R_2 could be computed according to Equation 3. Since $E_2 = R_2/\tau_2$, the value of E_2 could also be derived. From the values of $P_{\text{Tr},\text{max}}$, P_1 , $P_{\text{Visc},\text{max}}$ and $P_{\text{Rs},\text{st}}$ the following standard respiratory mechanics variables were computed [4]: 1) interruptor resistance ($R_{\text{int}} = (P_{\text{Tr},\text{max}} - P_1) / V'$); 2) $R_{\text{Visc}} = P_{\text{Visc},\text{max}} / V'$; and 3) static and dynamic elastances of the respiratory system ($E_{\text{Rs},\text{st}} = P_{\text{Rs},\text{st}} / V_{\text{T}}$ and $E_{\text{Rs},\text{dyn}} = P_1 / V_{\text{T}}$).

Multiple-breath method

The isoflow occlusion method was used, as previously described in detail [3, 4]. Under the same baseline conditions, four-second end-inspiratory occlusions were performed at four or five different inflation volumes by intermittently changing τ while keeping the basal inflation V' constant. The corresponding occluded inflation volumes ranged from $0.3\text{--}1.25 \text{ L}$. These tests were repeated three times. At each occlusion volume, the values of R_{Visc} was obtained and, together with the corresponding values of V' and τ , were fitted to Equation 2 to obtain R_2 and τ_2 . The investigation was approved by the local Ethics Committee and informed consent was obtained from each individual or their next of kin.

Statistical analysis

Regression analysis was performed using the least squares method. The paired t-test was used to compare the data of the first single-breath test with the corresponding average values obtained as the means of three repeated single-breath tests. The unpaired t-test was used to compare the present data with those of D'ANGELO *et al.* [3]. Comparison between the results provided by single and multiple-breath methods was performed by means of the limits of agreement [16], as modified for small sample sizes [17]. The significance level was established at $p < 0.05$.

Results

Table 2 depicts the values of R_{int} of the respiratory system ($R_{\text{Rs},\text{int}}$), R_{Visc} , $E_{\text{Rs},\text{st}}$ and $E_{\text{Rs},\text{dyn}}$, obtained with the first single-breath test (SB1) and the average of three repeated single-breath tests (SB3) in the normal subjects and ALI patients. There was no significant difference obtained between the SB1 and SB3 results. With SB3, the mean ($\pm \text{SD}$) intranormal subject and intra-ALI patient coefficients of variation of $R_{\text{Rs},\text{int}}$, R_{Visc} , $E_{\text{Rs},\text{st}}$ and $E_{\text{Rs},\text{dyn}}$ were $24 \pm 12\%$; $6 \pm 6\%$; $2 \pm 1\%$ and $2 \pm 2\%$, and $31.1 \pm 19\%$; $16.6 \pm 8.7\%$; $7.2 \pm 5.6\%$ and $5.2 \pm 4\%$, respectively. In all subjects, the data closely fitted Equation 2, the correlation coefficients (r) being highly significant ($p < 0.001$). The values of r ranged $0.883\text{--}0.990$ in the normal subjects and $0.871\text{--}0.981$ in ALI patients. The values of τ_2 , R_2 , and E_2 obtained with SB1 and SB3 in the normal subjects and ALI patients are given in table 3. There was no significant difference between the SB1 and SB3 results. With SB3, the mean ($\pm \text{SD}$) intranormal subject and intra-ALI patient coefficients of variation of τ_2 , R_2 , and E_2 were $10 \pm 8\%$, $7 \pm 5\%$ and $8 \pm 9\%$,

Table 2. – Respiratory mechanics variables of normal subjects (n=10) and patients with acute lung injury (ALI) (n=6) obtained using the single-breath method

	Normal subjects				ALI patients			
	$E_{rs,st}$ cmH ₂ O·L ⁻¹	$E_{rs,dyn}$ cmH ₂ O·L ⁻¹	$R_{rs,int}$ cmH ₂ O·L ⁻¹ ·s ⁻¹	R_{visc} cmH ₂ O·L ⁻¹ ·s ⁻¹	$E_{rs,st}$ cmH ₂ O·L ⁻¹	$E_{rs,dyn}$ cmH ₂ O·L ⁻¹	$R_{rs,int}$ cmH ₂ O·L ⁻¹ ·s ⁻¹	R_{visc} cmH ₂ O·L ⁻¹ ·s ⁻¹
SB1	18.8±3.4	22.4±3.7	1.49±0.81	2.88±0.65	23.3±8.4	30.1±14.7	4.14±2.12	4.36±1.28
SB3	18.8±3.5	22.3±3.8	1.56±0.86	2.98±0.64	22.8±8.7	30.7±15.1	3.91±1.52	4.58±1.32

Values are presented as means±SD. SB1: first single-breath test; SB3: average of three single-breath tests; $E_{rs,st}$: static elastance of the respiratory system; $E_{rs,dyn}$: dynamic elastance of the respiratory system; $R_{rs,int}$: interrupter resistance of the respiratory system; R_{visc} : viscoelastic resistance.

and 14.4±10%, 15.6±12.9% and 15.5±6.3%, respectively. Table 3 also depicts the mean values of τ_2 , R_2 , and E_2 obtained with the multiple breath method. The mean differences (±SD) of τ_2 , R_2 , and E_2 in normal subjects were -0.09±0.42 s, -0.19±0.66 cmH₂O·L⁻¹ and 0.27±0.66 cmH₂O·L⁻¹·s⁻¹, respectively. The mean differences (±SD) of τ_2 , R_2 , and E_2 in ALI patients were -0.11±0.24 s, -1.13±1.10 cmH₂O·L⁻¹·s⁻¹, -0.19±1.43 cmH₂O·L⁻¹, respectively. No lack of agreement could be detected between the two methods for all variables in normal subjects and in ALI patients.

Figure 2a depicts the relationships between the average values of R_{visc} and π obtained with the multiple-breath method in the 10 normal subjects and six ALI patients, together with those predicted according to Equation 2, using the individual values of the viscoelastic constants obtained with the single-breath method (both SB1 and SB3). Figure 2b depicts the corresponding changes in elastance of the respiratory system (ΔE_{rs}). The latter relationship was obtained according to the following equation [4]:

$$\Delta E_{rs} = P_{visc,max} / V = R_2 V' (1 - e^{-t/\tau_2}) / V \quad (6)$$

where V is inflation volume. Equation 6 is obtained by dividing both sides of Equation 3 by V . Also shown on the right ordinate of fig. 2b is the ratio $E_{rs,dyn}/E_{rs,st}$ in the normal subjects and in ALI patients, where $E_{rs,dyn}$ is the sum of ΔE_{rs} and $E_{rs,st}$. In these computations, the average values of $E_{rs,st}$ found with the single-breath method in the 10 normal subjects (18.8 cmH₂O·L⁻¹) and in the six ALI patients (22.75 cmH₂O·L⁻¹) were used.

Discussion

Viscoelastic constants of the respiratory system

The standard mechanics variables were obtained during single-breath RAO manoeuvres performed at baseline lung inflation volume (fig. 1) [3–5]. The present investigation shows that the viscoelastic constants of the respiratory

system can also be derived from the same manoeuvre. This method is reproducible and does not require many repeated occlusion tests, as is the case for the isoflow and isovolume multiple-breath methods previously used [3–5]. Furthermore, this analysis is based on Equations 3 and 5, which are independent of $R_{rs,int}$ and $E_{rs,st}$. Accordingly, the estimates of the viscoelastic constants obtained with the single-breath method are not affected by the volume dependence of $E_{rs,st}$ or the volume and flow dependence of $R_{rs,int}$ [3]. As with the multiple-breath method, the viscoelastic constants may be obtained from measurements of pressure at the airway opening instead of P_{tr} [3]. The values of the viscoelastic constants obtained with the single-breath method were not significantly different from those obtained with the isoflow multiple-breath method. Using the isoflow multiple-breath method, D'ANGELO *et al.* [3] determined the viscoelastic constants of the total respiratory system in 16 normal young subjects under similar experimental conditions to those of the present study. Their values of τ_2 , R_2 , and E_2 amounted to 0.96±0.2 s, 4.60±0.81 cmH₂O·L⁻¹·s⁻¹ and 5.10±1.57 cmH₂O·L⁻¹, respectively, and are not significantly different from those obtained in the present study with the multiple-breath method. Using a modified multiple-breath method, JONSON *et al.* [18] determined the viscoelastic constants of the respiratory system in six normal, anaesthetized paralysed subjects, which also do not differ significantly from the present results.

As in normal subjects, in ALI patients the viscoelastic constants could be obtained by the single-breath method and the values were not significantly different from those obtained by the multiple breath method. In patients and animal models of lung disease, τ_2 , R_2 , and E_2 represent not only viscoelasticity, but also the mechanical inhomogeneities of the lung. In this line, the values found in the present ALI patients should be regarded as encompassing viscoelasticity and/or mechanical inhomogeneities of the respiratory system. In ALI patients the values of R_2 , and E_2 were significantly higher than in normal subjects while τ_2 was not significantly different. This suggest that most

Table 3. – Viscoelastic time constant (τ_2), resistance (R_2), and elastance (E_2) of the respiratory system in normal subjects (n=10) and in patients with acute lung injury (ALI) (n=6)

	Normal subjects			ALI patients		
	τ_2 s	R_2 cmH ₂ O·L ⁻¹ ·s ⁻¹	E_2 cmH ₂ O·L ⁻¹	τ_2 s	R_2 cmH ₂ O·L ⁻¹ ·s ⁻¹	E_2 cmH ₂ O·L ⁻¹
SB1	1.13±0.17	4.82±1.28	4.25±0.65	1.31±0.51	9.79±6.57	7.43±2.96
SB3	1.17±0.19	5.09±1.25	4.38±0.77	1.29±0.39	9.20±4.27	7.27±2.80
MB	1.08±0.37	4.89±1.32	4.66±0.83	1.40±0.50	10.33±4.99	7.45±2.12

Values are presented as means±SD. SB1: first single-breath test; SB3: average of three single-breath tests; MB: multiple-breath method.

Fig. 2. — Average relationships of a) viscoelastic resistance (R_{visc}) and b) elastance of the respiratory system (ΔE_{rs}) to inspiratory time in 10 normal subjects and six patients with acute lung injury (ALI) obtained using the single-breath method (--- : first test; : average of three tests) and using the multiple-breath method (—). In ALI patients, maximal viscoelastic pressure ($P_{\text{visc,max}}$) includes pressure losses due to time-constant inhomogeneity within the lung. Also shown on the right ordinate of b) are the changes in dynamic elastance of the respiratory system ($E_{\text{rs,dyn}}$ = elastance of the respiratory system ($E_{\text{rs,st}}$) + ΔE_{rs}) of normal subjects and ALI patients expressed as a fraction of the $E_{\text{rs,st}}$. A: ALI patients; N: normal subjects.

of the increase in R_2 , and E_2 in ALI patients was due mainly to a reduction in lung volume. Indeed, according to the "baby lung" concept of GATTINONI *et al.* [19], in ALI patients the aerated parts of the lung should be normal (as reflected by the unchanged τ_2), while the increase in R_2 , and E_2 should simply reflect reduced lung volume.

This analysis, which was based on a linear viscoelastic model, should not be regarded as a complete and perfect representation of respiratory mechanics. More complex nonlinear viscoelastic [20] and viscoplastoelastic models [21] have been used to explain the volume and time dependency of energy dissipation within the respiratory system. Nevertheless, the linear viscoelastic model has been shown to provide an accurate description of the time dependency of resistance and elastance over the lung volume range used in the present study [3–5]. In fact, the present results show that the t_i dependency of resistance and elastance of the total respiratory system can be predicted with reasonable accuracy from the values of viscoelastic constants obtained with the single-breath method, as shown in figure 2. This is especially true for the range of t_i commonly used during mechanical ventilation (up to 2 s). Thus, with the single-breath method, not only can the values of R_{visc} and $E_{\text{rs,dyn}}$ during baseline ventilation be obtained, but the t_i dependence of these variables can also be provided (fig. 2).

$R_{\text{rs,int}}$ and $E_{\text{rs,int}}$

In the present investigation $R_{\text{rs,int}}$ amounted to 1.49 ± 0.81 cmH₂O·L⁻¹·s⁻¹ with SB₁ and 1.56 ± 0.86 cmH₂O·L⁻¹·s⁻¹ with SB₃. These values were significantly lower ($p < 0.02$) than those found in 16 normal young subjects by D'ANGELO *et al.* [3]. These authors, however, did not obtain $R_{\text{rs,int}}$ directly from measurements of P_{tr} , as in the present study. Instead, they derived $R_{\text{rs,int}}$ indirectly by correcting the drop in airway opening pressure after end-inspiratory occlusion for the resistive pressure drop due to the endotracheal tube, which was measured *in vitro*. This indirect method, however, is not accurate [22]. Indeed, in a subsequent study based on P_{tr} measurements in 12 normal sub-

jects, D'ANGELO *et al.* [11] found values of $R_{\text{rs,int}}$ similar to those of the present study (1.54 ± 0.46 cmH₂O·L⁻¹·s⁻¹). In the present study, the mean intrasubject coefficient of variation of $R_{\text{rs,int}}$ was relatively high, amounting to $24 \pm 12\%$. This reflects the fact that in some of the subjects at inflation flow of 0.5 L·s⁻¹, the values of $P_{\text{max}} - P_1$ were relatively low in relation to the cardiac artefacts in P_{tr} . In such instances, accurate assessment of $R_{\text{rs,int}}$ requires ensemble averaging of several end-inspiratory occlusion records [11]. The present values of $E_{\text{rs,st}}$ were similar to those found in two previous studies on normal young subjects under similar experimental conditions [4, 11], but significantly higher than those found by D'ANGELO *et al.* [3]. The reason for this discrepancy is not clear.

The single-breath method was also successfully applied to ALI patients who were selected according to the North American-European Consensus Conference [13]. The definition of ALI encompasses a wide range of severity of sickness, which is reflected in the marked interindividual variation in respiratory mechanics values in the ALI patients (tables 2 and 3).

Conclusions

The results show that with the single-breath method it is possible to derive not only the standard mechanics data but also the inflation time-dependence of the viscoelastic resistance and the dynamic elastance of the respiratory system as well as the viscoelastic constants of the respiratory system in both normal subjects and patients with acute lung injury.

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