

## Modelling of passive expiration in patients with adult respiratory distress syndrome

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**ABSTRACT:** The time-course of volume change during passive expiration preceded by an end-inspiratory hold was studied with a biexponential model in six adult respiratory distress syndrome (ARDS) patients.

We measured the initial volumes and time constants of the fast ( $\tau_1$ ), and the slow ( $\tau_2$ ) compartments of expiration, as well as the static elastance of the respiratory system. The results were compared to those of 11 normal subjects.

We observed that: 1) the biexponential model fitted closely the volume decay; 2) the fast compartment was responsible for  $81 \pm 7\%$  (ARDS) versus  $84 \pm 10\%$  (controls) of the total volume exhaled, with  $\tau_1 = 0.35 \pm 0.11$  s (ARDS) versus  $0.50 \pm 0.22$  s (controls); 3) the slow compartment contributed only  $19 \pm 6\%$  (ARDS) versus  $16 \pm 7\%$  (controls), with  $\tau_2 = 4.67 \pm 2.38$  s (ARDS) versus  $3.27 \pm 1.54$  s (controls); and 4) static elastance was higher in ARDS patients.

The findings could be explained in terms of a four parameter viscoelastic model of the respiratory system.

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The first mechanical model of the respiratory system was introduced in 1950 by Orris *et al.* [1]. It consisted of a single compartment of constant elastance ( $E_{rs}$ ), served by a pathway of constant resistance ( $R_{rs}$ ), and hence was characterized by a single energy storage time constant ( $\tau_{rs} = R_{rs}/E_{rs}$ ). Based on this model, the time-course of volume ( $V$ ), during the portion of passive deflation corresponding to decreasing flow, should be described by a single-exponential function [2]:

$$V = V_0 \cdot e^{-t/\tau_{rs}} \quad (1)$$

where  $t$  is time and  $V_0$  is initial volume above the relaxation volume of the respiratory system. However, recent studies on normal anaesthetized-paralysed dogs [3], and humans [4], have shown that passive expiration preceded by an end-inspiratory pause is better described by a double-exponential function:

$$V = A_1 \cdot e^{-t/\tau_1} + A_2 \cdot e^{-t/\tau_2} \quad (2)$$

where  $A_1$  and  $A_2$  are the initial volumes of the fast and slow compartment,  $A_1 + A_2 = V_0$  and  $\tau_1$  and  $\tau_2$  are the corresponding time constants. In normal humans [4, 5], and

dogs [3, 6],  $\tau_2$  is much longer than  $\tau_1$ . This not only affects the time-course of lung emptying (Eq. 2) but also has profound implications in terms of work of breathing [7], and frequency-dependence of resistance and compliance of the lungs and chest wall [8].

In the present study, we have determined the constants in Equation (2) in intubated paralysed patients with adult respiratory distress syndrome (ARDS), together with static elastance of the respiratory system ( $E_{st,rs}$ ). Our results are interpreted in terms of a viscoelastic model of the respiratory system [9].

### Patients and methods

We studied six supine patients with ARDS, who were admitted into the medical intensive care unit. In defining ARDS we used the criteria of PEPÉ *et al.* [10], namely: 1) presence of an illness known to predispose to ARDS; 2) presence of infiltrates on chest radiography compatible with pulmonary oedema; 3) pulmonary arterial wedge pressure  $< 18$  mmHg; 4) need for an inspired  $O_2$  fraction ( $F_{iO_2}$ )  $> 50\%$  and/or positive end-expiratory pressure (PEEP) to keep arterial oxygen tension ( $P_{aO_2}$ )  $> 50$  mmHg

(6.7 kPa); and 5) negative history of lung disease and no other explanation for these findings. They had no cardiac failure as judged by bidimensional echocardiography. The clinical entry data of the patients are shown in table 1. The mean lung injury score computed according to MURRAY *et al.* [11] was >2.5, indicating a severe degree of acute lung injury in all patients. The duration of mechanical ventilation was, on average, 4 days.

The investigation was approved by the Institutional Ethics Committee, and informed consent was obtained from the next of kin.

Patients were intubated with Portex cuffed endotracheal tubes (ET) ranging in internal diameter (ID) from 7–8 mm, and mechanically-ventilated with  $F_{iO_2}$  ranging from 0.4–0.8 (table 1). After adequate sedation with flunitrazepam (Narcozep®), the patients were paralysed with 4 mg *i.v.* of vecuronium bromide (Norcuron®), followed by additional aliquots of 2 mg every 10 min. They were curarized to assure respiratory muscle relaxation for the respiratory mechanics measurements.

were  $0.996 \pm 0.03$  and  $0.994 \pm 0.006$  for thorax and abdomen, respectively. Partitioning was calculated as the ratio of thorax-to-abdomen RIP deflections, after insufflation with a 2 l syringe of volumes ranging from 200–1,200 ml, maintained for 15 s. Partitioning was widely variable among patients (0.40–1.11) but highly reproducible in a given patient, with a coefficient of variation of  $6.4 \pm 2.9\%$  ( $\pm SD$ ). The same authors have recently shown [17] that in paralysed, intubated patients, without thoracoabdominal surgery or X-ray asymmetry, the respiratory system moves with a single degree of freedom during passive ventilation, with no variation in thoracoabdominal partitioning of tidal volume over a large volume range for any given patient. In consequence, volume variations and time constants can be reliably measured in paralysed patients with a single-coil RIP. This conclusion cannot be extrapolated to non-paralysed patients. Therefore, the use of a single-coil RIP was justified in our study. The coil was fixed on the skin of the abdomen at mid-distance from the iliac crest and the axilla. The direct current

Table 1. – Anthropometric data and clinical findings of ARDS patients

Pt no.	Sex	Age yrs	Wt kg	Ht cm	Days after intubation	Pao <sub>2</sub>		Fio <sub>2</sub>	Diagnosis	ID mm	Final course
						mmHg	kPa				
1	M	16	60	176	4	55.5	7.4	0.4	Acute leukaemia, BBP	7.5	S
2	F	51	46	164	5	49.5	6.6	0.6	Acute leukaemia, BBP and shock	7.5	D
3	F	29	56	162	4	59.4	7.9	0.6	ARF (paraquat self-poisoning), sepsis and shock	7.5	D
4	F	50	46	163	6	53.2	7.1	0.6	ARF (CO poisoning and serious burns), sepsis and shock	8.0	D
5	F	60	56	165	4	59.3	7.9	0.6	BBP, sepsis, and shock	7.0	D
6	M	37	77	176	2	56.0	7.5	0.8	Acute leukaemia, BBP	8.0	D

ID: internal diameter of endotracheal tube; S: survived; D: died; BBP: bilateral bacterial pneumonia; ARF: acute renal failure; Pao<sub>2</sub>: arterial oxygen tension; Fio<sub>2</sub>: fractional inspiratory oxygen; ARDS: adult respiratory distress syndrome; CO: carbon monoxide.

Respiratory muscle relaxation was thought to be achieved when there was no breath-by-breath variation in end-expiratory thoracic volume and airway pressure (Paw), and when a plateau of Paw was observed during end-inspiratory airway occlusion [12]. Changes in thoracic volume were measured by respiratory inductive plethysmography (RIP) (Respiograph TM, NIMS, Miami Beach, FL, USA). Since the patients were paralysed, the respiratory system behaved to a good degree of approximation with a single degree of freedom [13, 14] and, hence, a single RIP coil (direct current mode) was used. It has already been demonstrated in paralysed subjects [14, 15] that one-coil RIP allows volume correction for gas exchange, which takes place throughout apnoea and, thus, can be made time-independent, allowing for reliable thoracopulmonary pressure-volume (PV) curves to be obtained, and for continuous monitoring of end-expiratory volume changes.

Moreover, DALL'AVA-SANTUCCI *et al.* [16] showed that the use of one-coil RIP is justified only if thoracopulmonary partitioning is constant in a given patient. In a study on eight patients with various lung diseases, these authors used a two-coil RIP to study thoracopulmonary partitioning. Correlation coefficients of calibration lines

(DC) mode was used in order to monitor the end-expiratory level of the respiratory system. Since in DC mode the oscillator drift is sensitive to temperature [18], we waited for 30 min before taking any measurements to allow for thermal equilibrium. Non-cumulative calibration was performed by incremental inflation with a hand-driven 2 l syringe, as described previously [14, 15]. Airway pressure was measured at the proximal end of the endotracheal tube, with a differential pressure transducer (Validyne M.P.15,  $\pm 60$  cmH<sub>2</sub>O, Northridge, CA, USA). Paw and RIP outputs were recorded on a two-pen potentiometric recorder (2 YT Sefram, Valizy, France). The recorder and the RIP had a time constant of 0.01 and 0.005 s, respectively.

A two-way tap was used to disconnect the patient from the ventilator, and for airway occlusion. During passive deflation, the patients were disconnected from the ventilator and expired freely at barometric pressure, thus avoiding any equipment resistance, except for the endotracheal tube.

The inflation volume was initially set at 10 ml·kg<sup>-1</sup>, but was subsequently adjusted to keep arterial blood gases within normal limits. As a result, the baseline tidal volume (V<sub>T</sub>) ranged from 5–12 ml·kg<sup>-1</sup>. The

baseline respiratory frequency ranged between 15–18 cycles·min<sup>-1</sup>. All patients were studied at zero end-expiratory airway pressure (ZEEP). PEEP (12.7±3.7 cmH<sub>2</sub>O) was removed 20–30 min before the study, and patients were judged to have reached a steady state by stability of respiratory mechanics and blood gas records.

#### Procedure

After a period of stable mechanical ventilation, end-inspiratory airway occlusions were performed with the manual tap. During the ensuing period of apnoea (5–6 s), relaxation of the respiratory muscles was shown by the appearance of a plateau on the tracheal pressure tracing. The occlusion was then rapidly released, and the patients allowed to expire freely into the atmosphere, until full expiration was achieved, *i.e.* until the RIP signal was steady for at least 1.5 s. A steady end-expiratory RIP signal was taken as evidence that the expiration was complete [19]. Two end-inspiratory occlusions were performed in each patient. Each occlusion was preceded by 10 regular mechanical inflations with baseline V<sub>T</sub>. Prior to each study, the lungs were inflated with three cumulative baselines V<sub>T</sub>s, by occluding the expiratory line of the ventilator for three breaths, in order to produce a constant previous lung volume history.

#### Data analysis

As plateau pressure during occlusion was reached in <5s, tracheal pressure at 5–6 s was taken to represent the end-inspiratory static elastic recoil pressure of the total respiratory system (P<sub>el,rs</sub>). During this period, the contribution of reduction in pressure due to volume loss by continuing gas exchange should be negligible [15].

The static elastance of the total respiratory system (Est,rs) was computed by dividing the end-inspiratory static tracheal pressure by the volume expired into the atmosphere. Individual curves (two curves for each patient) relating RIP volume and time were digitized at intervals of 0.1 s (10 Hz), until end-expiration.

In order to assess whether our results best fitted mono- or biexponential functions, the experimental data were analysed in terms of "goodness of fit". The mono-exponential model was compared with the biexponential one by analysis of variance, based on the least-squares sum calculated from each curve fitting: the biexponential model was preferred to the monoexponential one when the Fisher test indicated a significant result ( $p < 0.05$ ) [20]. Decay slopes ( $\tau_1$  and  $\tau_2$ ) obtained from the experiments were compared by an analysis of variance (ANOVA). In all patients the biexponential model better fitted the data than the monoexponential one, as indicated by a significant difference by Fisher's coefficient ( $p < 0.05$ ). Moreover, correlation coefficients ranged between 0.991–0.999 for the biexponential model, and 0.953–0.988 for the monoexponential one.

Parameter estimation according to Equation (2) was performed using an optimized computer algorithm, based on a Gauss-Newton procedure, using the least-squares methods (Ph. D'Atis, Programme Triomphe, Laboratoire d'Informatique Médicale, Faculté de Médecine, CHU Dijon, 211000, France).

#### Statistical analysis

Results were expressed as mean±SD. Statistical analysis was performed using Student's paired and unpaired *t*-tests. Regression analysis was done with the least-squares method. Significance was accepted at  $p < 0.05$ .

Results were compared to similar data obtained on 11 subjects with normal lungs [4].

### Results

Table 2 lists the individual values of V<sub>T</sub>, Est,rs and of the parameters in Equation (2). Each individual value is the mean of two determinations. There was no significant difference between duplicate measurements (Student's paired *t*-test). Est,rs amounted to 37.6±6.1 cmH<sub>2</sub>O·l<sup>-1</sup>.

Figure 1 depicts the time-course of volume decay during passive lung deflation in a representative patient.

Table 2. – Values of parameters of standard respiratory mechanics and of biexponential function of ARDS patients

Pt no.	V <sub>T</sub> ml	Est,rs cmH <sub>2</sub> O·l <sup>-1</sup>	A <sub>1</sub> ml	A <sub>2</sub> ml	$\tau_1$ s	$\tau_2$ s
1	350	36.5	274	75	0.28	2.78
2	445	38.5	388	58	0.52	8.33
3	622	32.9	560	64	0.43	6.67
4	540	32.0	431	106	0.26	3.70
5	493	36.5	358	134	0.36	4.35
6	596	49.0	451	145	0.24	2.17
Mean	508	37.6	410	97	0.35	4.67
SD	101	6.1	96	37	0.11	2.38

ARDS: adult respiratory distress syndrome; V<sub>T</sub>: tidal volume; Est,rs: static elastance of the respiratory system; A<sub>1</sub> and A<sub>2</sub>,  $\tau_1$  and  $\tau_2$ , coefficients of biexponential model fit (Eq. 2).

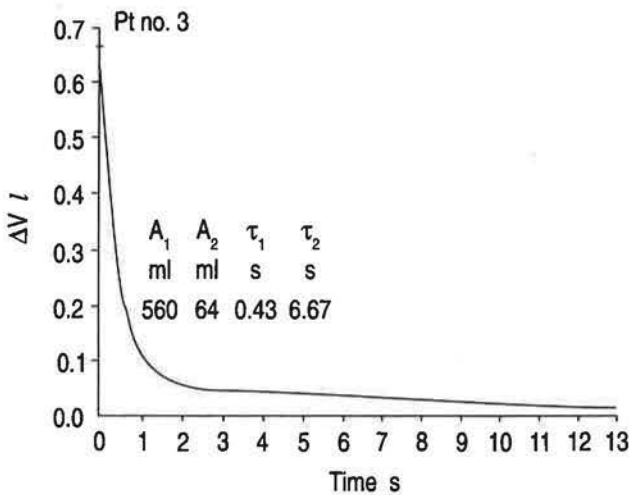


Fig. 1. - Relationship between changes in volume ( $\Delta V$ ) and time during passive expiration in a representative ARDS patient. Experimental points closely fit Equation 2 ( $r>0.99$ ). ARDS: adult respiratory distress syndrome;  $A_1$  and  $A_2$ ,  $\tau_1$  and  $\tau_2$ : coefficients of biexponential model fit (Eq. 2).

The change in volume ( $\Delta V$ ) as a function of time is well described by the biexponential model (Eq. 2), as indicated by the high value of the correlation coefficient ( $r>0.99$ ). Similar results were obtained in the other patients ( $r>0.99$ ). The term  $A_1 \cdot e^{-t/\tau_1}$  in Equation (2) represents the fast compartment, whilst the term  $A_2 \cdot e^{-t/\tau_2}$  identifies the slower compartment.

The time constant of the fast compartment ( $\tau_1$ ) was  $0.35 \pm 0.11$  s, and  $A_1$  amounted to  $81 \pm 7\%$  of  $V_T$ . The time constant of the slow compartment ( $\tau_2$ ) was  $4.67 \pm 2.38$  s and  $A_2$  amounted to  $19 \pm 6\%$  of  $V_T$ . On average,  $\tau_2$  was 13.3 times longer than  $\tau_1$ .

**Discussion**

The main finding of this study is that in ARDS patients the volume-time course during a passive expiration following an end-inspiratory pause can be adequately described by a biexponential function (Eq. 2). A similar behaviour was previously observed in anaesthetized paralysed dogs [3], and normal subjects [4], and was attributed to the viscoelastic properties of the respiratory system [3, 4]. Indeed, the present results are also consistent with the viscoelastic model of the respiratory system of BATES *et al.* [21], which stems from pioneering work of MOUNT [22]. In its simplest form, this model consists of two compartments in parallel: a dashpot, which in humans represents airway resistance ( $R_{aw}$ ) [8], and a Kelvin body (fig. 2). The latter consists of a spring representing the static elastance of the respiratory system ( $Est,rs$ ) in parallel with a Maxwell body, *i.e.* a spring ( $E_2$ ) and a dashpot ( $R_2$ ) arranged serially.  $E_2$  and  $R_2$  represent the elastance and resistance of the viscoelastic (stress adaptation) units within the pulmonary and chest wall tissues. The corresponding viscoelastic time constant ( $\tau_2$ ) is given by the ratio  $R_2/E_2$ . The distance between the two

horizontal bars is analogue of lung volume ( $V$ ), and the tension between these bars is analogue of  $P_{aw}$ . The model in figure 2 is not intended to be a complete and perfect representation of respiratory system behaviour. Indeed, the limitations of this simplistic model have been discussed in detail previously [5, 6, 8, 21, 23]. At the moment, the precise structural basis of the viscoelastic elements remains to be elucidated. Nevertheless, the model in figure 2 appears to be useful for explaining respiratory system behaviour.

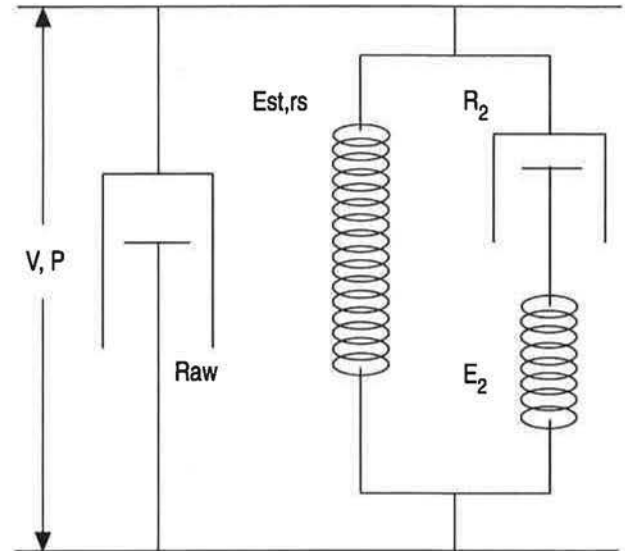


Fig. 2. - Scheme of spring-and-dashpot model for interpretation of respiratory dynamics. Respiratory system consists of airway resistance ( $R_{aw}$ ), in parallel with standard elastance ( $Est,rs$ ), and with a series spring-and-dashpot body ( $E_2$ ,  $R_2$ , respectively) that represents stress adaptation units. Distance and tension between two horizontal bars are analogue of lung volume ( $V$ ) and of pressure at airway opening ( $P$ ), respectively, (modified from [21]).

Under elastic equilibrium conditions ( $P_{aw}=0$ ), the tension in both springs in figure 2 is nil, and  $V$  corresponds to the relaxation volume of the respiratory system ( $V_r$ ). When the model is elongated slowly, the dashpot  $R_2$  is given time to move and dissipate the tension in spring  $E_2$ . In the limit, at very low speed of elongation (analogue to very low flow), the spring  $E_2$  should remain at its elastic equilibrium length ( $l_0$ ) at which its tension is nil. In this case, the relationship between the elastic pressure of the respiratory system ( $P_{el,rs}$ ) and the inflation volume will be given by:

$$P_{el,rs} = P_{st,rs} = Est,rs \Delta V \tag{3}$$

where  $\Delta V$  is volume change relative to  $V_r$ ,  $P_{st,rs}$  is static end-inspiratory pressure. In contrast, at higher elongation speeds (equivalent to higher inflation flows), there will be insufficient time for the tension in spring  $E_2$  to be entirely dissipated through the dashpot  $R_2$ . In this case  $P_{el,rs}$ , at any given  $\Delta V$ , will be necessarily higher than  $P_{st,rs}$ . In the limit (*i.e.* when inflation time is very short in relation to  $\tau_2$ ), the dashpot  $R_2$  will not move at all, and hence the tension in spring  $E_2$  will equal  $E_2 \Delta V$ .

In this case, springs  $E_{1,rs}$  and  $E_2$  being in parallel, the relationship between  $P_{el,rs}$  and  $\Delta V$  will be given by:

$$P_{el,rs} = (E_{1,rs} + E_2) \Delta V \quad (4)$$

If a "flow interruption" manoeuvre (*i.e.* a pause) is performed at a given  $\Delta V$ , by halting the relative movement of the two horizontal bars for a time  $> 3 \tau_2$ , the spring  $E_2$  will gradually return to  $l_0$ , *i.e.* spring  $E_2$  will now exert zero tension at a volume equal to  $V_r$  plus  $\Delta V$ . Under these conditions, the end-inspiratory  $P_{el,rs}$  will be given by Equation (3), and passive expiration will necessarily include a slow compartment ( $A_2$ ), representing the gradual relaxation of spring  $E_2$  until it returns to  $l_0$  at  $V_r$ .

According to the above analysis, the magnitude of  $A_2$  should vary with the speed of inspiration and the duration of the end-inspiratory pause: the faster the speed of inspiration and/or the shorter the duration of the pause, the smaller should be  $A_2$  for a given  $\Delta V$ . This is because, with fast inspiration the dashpot  $R_2$  will not have time to move at all, whilst with a short pause the spring  $E_2$  will not have sufficient time to return to  $l_0$ . In the limit, during passive lung deflation after a fast inspiration without any end-inspiratory pause, there should be no slow compartment ( $A_2 = 0$ ). On the other hand, during slower inspiration the dashpot  $R_2$  will have time to move [5, 6, 8, 9, 19] and, hence, during the following expiration there will be a slow compartment even without any end-inspiratory pause. In short, the magnitude of  $A_2$  depends on the previous volume history.

Our measurements were obtained following a 5–6 s end-inspiratory pause, a time long enough for spring  $E_2$  to attain relaxation in both normal subjects [5, 8], and ARDS patients [23]. Accordingly, in our study,  $A_2$  should reflect maximal values for a given inflation volume. In our ARDS patients it amounted to  $19 \pm 6\%$  of  $V_T$  and did not differ significantly from the values ( $16 \pm 7\%$  of  $V_T$ ) obtained using the same technique in 11 comatose (self-poisoning) subjects with presumably normal lungs [4]. The values of  $\tau_1$  and  $\tau_2$  obtained in our ARDS patients were also similar to those obtained in the 11 comatose subjects ( $\tau_1$ :  $0.35 \pm 0.11$  versus  $0.50 \pm 0.22$  s;  $\tau_2$ :  $4.67 \pm 2.38$  versus  $3.27 \pm 1.54$  s). In this connection, it should be noted that  $E_{st,rs}$  was significantly higher in the ARDS patients ( $37.6 \pm 6.1$  versus  $20.1 \pm 6.1$   $\text{cmH}_2\text{O} \cdot \text{l}^{-1}$ ) ( $p < 0.001$ ). This is in line with previous reports [23–25].

The absence of a significant difference in  $\tau_2$  between ARDS patients and subjects with normal lungs suggests that in ARDS the tissues subtending the aerated and ventilated lung units exhibit relatively normal viscoelastic behaviour. This fits the notion that ARDS is characterized by a bimodal distribution: 1) normal aerated and ventilated units; and 2) abnormal non-aerated and non-ventilated units [26]. Indeed, in a such case,  $\tau_2$  of the remaining normal lung units should be the same as in normal subjects.

However, in some of our ARDS patients,  $\tau_2$  was unduly long, probably reflecting alteration in viscoelastic behaviour due to a modification of the rheological properties of the pulmonary tissues. Such prolongation of  $\tau_2$  probably contributes to the intrinsic PEEP and the dy-

namic pulmonary hyperinflation, which are observed in some ARDS patients [24, 27].

Based on the linear viscoelastic model in figure 2, BATES and co-workers [9, 28] developed equations for predicting  $A_1$ ,  $A_2$ ,  $\tau_1$  and  $\tau_2$  for passive expiration following an end-inspiratory pause (see Appendix). Based on these equations, and using the average values of the viscoelastic constants in figure 2 determined by EISSA *et al.* [23] in eight ARDS patients, the values of  $A_1$  and  $A_2$  amounted to 81.4 and 18.6% of  $V_T$ , respectively. This is very close to the corresponding values found in the present study (81 and 19% of  $V_T$ , respectively). The computed values of  $\tau_1$  and  $\tau_2$  averaged, respectively, 0.12 and 2.90 s, as compared to 0.35 and 4.67 s found in the present study. Since in the ARDS patients of the present study  $E_{st,rs}$  ( $37.6 \pm 6.1$   $\text{cmH}_2\text{O} \cdot \text{l}^{-1}$ ) was not significantly different from that of EISSA *et al.* [23] ( $32.2 \pm 7.9$   $\text{cmH}_2\text{O} \cdot \text{l}^{-1}$ ), this discrepancy (particularly that in  $\tau_1$ ) probably mainly reflects the fact that in our computations the substantial resistance of the endotracheal tubes [12] was not taken into account.

Apart from the aspects discussed above, the viscoelastic properties of the respiratory system have other important implications in terms of the dynamic behaviour of the respiratory system, because they confer time-dependency (frequency-dependence) of respiratory resistance and elastance [5, 6, 8, 21, 23, 29], and increase the dynamic work of breathing [7].

It should be noted that the model in figure 2 does not take into account time constant inhomogeneities within the lung, *i.e.* "pendelluft" [30]. Whilst in normal subjects this mechanism probably plays a negligible role [5, 8, 30, 31], this may not be the case in ARDS patients [23]. At present, it is not possible to differentiate between the effect of viscoelastic properties and "pendelluft" on respiratory system behaviour.

### Appendix

The behaviour of the model of respiratory system in figure 2 during relaxed expiration after an end-inspiratory pause, is characterized by a second-order differential equation, the solutions of which are biexponential curves [9, 28]. The exponential coefficients ( $\tau_1$  and  $\tau_2$ ) of these curves can be calculated by the following equation [9, 28]:

$$\tau_{2,1} = \frac{R_1 E_1 + R_1 E_2 + R_2 E_1 \pm \sqrt{(R_1 E_1 + R_1 E_2 + R_2 E_1)^2 - 4 R_1 R_2 E_1 E_2}}{2 E_1 E_2} \quad (5)$$

where  $R_1 = R_{aw}$  and  $E_1 = E_{st,rs}$  in figure 2.

The corresponding constants  $A_1$  and  $A_2$  are given by:

$$A_1 = P_{st,rs} (E_1 \tau_2 - R_1) \tau_1 / [R_1 E_1 (\tau_2 - \tau_1)] \quad (6)$$

$$A_2 = P_{st,rs} / E_1 - A_1 \quad (7)$$

where  $P_{st,rs}$  is static end-inspiratory pressure.

Since  $V_T = P_{st,rs}/E_1$ , it follows that the  $A_1/V_T$  ratio is obtained by dividing Equation (6) by  $P_{st,rs}/E_1$ :

$$A_1/V_T = (E_1 \tau_2 - R_1) \tau_1 / R_1 (\tau_2 - \tau_1) \quad (8)$$

Equation (8) indicates that, according to the model in figure 2, the  $A_1/V_T$  ratio is independent of the magnitude of  $V_T$ . The same is obviously also true for  $A_2/V_T$ .

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